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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: My Chau Tran Examiner #: 78933 Date: 2/27/02
Art Unit: 1641 Phone Number 30 5-6999 Serial Number: 09/755,701
Mail Box and Bldg/Room Location: CM1, 8A16 Results Format Preferred (circle): PAPER DISK E-MAIL
7E12

If mor than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Enhanced transport using membrane disruptive agents

Inventors (please provide full names): Allan S. Hoffman, Patrick S. Stayton, ~~and Kiren Murthy~~ and Kiren Murthy

Earliest Priority Filing Date: 1/7/2000

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please perform: 1) Inventor search
~~2) Search attached claims~~
2) Search attached claims

Thank you

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Searcher: Point of Contact: Alexandra Waclawiw Technical Info. Specialist CM1 6A02 Tel: 308-4491
Searcher Phone #:
Searcher Location:
Date Searcher Picked Up: 3-7-02
Date Completed: 3-7-02
Searcher Prep & Review Time: 9
Clerical Prep Time:
Online Time: 48

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic V
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN
Dialog (1)
Questel/Orbit 5
Dr.Link
Lexis/Nexis 36
Sequence Systems
WWW/Internet
Other (specify)

52
45-7
2
41
48

PTO-1590 (8-01)

Inventor Search

Tran 09/755,701

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=> fil biosis hcaplus wpids
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FILE 'WPIDS' ENTERED AT 10:27:57 ON 07 MAR 2002
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=> d que l6;d his l7-
L1          689 SEA "HOFFMAN A"/AU OR "HOFFMAN A S"/AU
L2          339 SEA "HOFFMAN ALLAN"/AU OR ("HOFFMAN ALLAN S"/AU OR "HOFFMAN
                ALLAN SACHS"/AU)
L3          218 SEA ("STAYTON P"/AU OR "STAYTON P S"/AU OR "STAYTON PARICK
                S"/AU OR "STAYTON PAT"/AU OR "STAYTON PAT S"/AU OR "STAYTON
                PATRICK"/AU OR "STAYTON PATRICK S"/AU OR "STAYTON PATRICK
                SEAN"/AU)
L4          582 SEA ("MURTHY N"/AU OR "MURTHY N B K"/AU OR "MURTHY N C"/AU OR
                "MURTHY N D A"/AU OR "MURTHY N G K"/AU OR "MURTHY N K"/AU OR
                "MURTHY N KRISHNA"/AU OR "MURTHY N L"/AU OR "MURTHY N L N"/AU
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                "MURTHY N V A"/AU OR "MURTHY N V ADINARAYANA"/AU OR "MURTHY N
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                "MURTHY N V S R"/AU OR "MURTHY N VISHNU"/AU)
L5           21 SEA "MURTHY NIREN"/AU
L6         1753 SEA (L1 OR L2 OR L3 OR L4 OR L5)



     (FILE 'BIOSIS, HCAPLUS, WPIDS' ENTERED AT 10:22:49 ON 07 MAR 2002)
L7           55 S L6 AND MEMBRAN?
L8           58 S TRANSPORT? AND L6
L9          105 S L7 OR L8
L10       90005 S  DISRUPT?
L11     1481201 S POLYMER##
L12          10 S L9 AND L10 AND L11
L13          13 S L9 AND L10
L14          37 S L9 AND (L10 OR L11)
L15          32 DUP REM L14 (5 DUPLICATES REMOVED)

     FILE 'BIOSIS, HCAPLUS, WPIDS' ENTERED AT 10:27:57 ON 07 MAR 2002

=> d bib ab 1-32

L15  ANSWER 1 OF 32  HCAPLUS  COPYRIGHT 2002 ACS       DUPLICATE 1
AN   2001:525957  HCAPLUS
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DN 135:127195
TI Enhanced **transport** of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**
IN **Hoffman, Allan S.; Stayton, Patrick S.; Murthy, Niren**
PA University of Washington, USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001051092	A2	20010719	WO 2001-US356	20010105
WO 2001051092	A3	20011206		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-174893 P 20000107
AB Compns. and methods for transport or release of therapeutic and diagnostic agents, metabolites or other analytes from cells, compartments within cells, or through cell layers or barriers are described. The compns. include a membrane barrier transport enhancing agent and are usually administered in combination with an enhancer and/or exposure to stimuli to effect disruption or altered permeability, transport or release. In a preferred embodiment, the compns. include compds. which disrupt endosomal membranes in response to the low pH in the endosomes but which are relatively inactive toward cell membranes (at physiol. pH, but can become active toward cell membranes if the environment is acidified below pH 6.8), coupled directly or indirectly to a therapeutic or diagnostic agent. Other disruptive agents can also be used, responsive to stimuli and/or enhancers other than pH, such as light, elec. stimuli, electromagnetic stimuli, ultrasound, temp., or combinations thereof. The compds. can be coupled by ionic, covalent or H bonds to an agent to be delivered or to a ligand which forms a complex with the agent to be delivered. Agents to be delivered can be therapeutic and/or diagnostic agents. Treatments which enhance delivery such as ultrasound, iontophoresis, and/or electrophoresis can also be used with the disrupting agents. For example, a terpolymer of dimethylaminoethyl methacrylate, Bu methacrylate, and styrene benzaldehyde was prepd. for the membrane-disruptive backbone which was then PEGylated with thiol-terminated monofunctional or heterofunctional PEGs. The acid-degradable linkage was a p-aminobenzaldehyde acetal.

L15 ANSWER 2 OF 32 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-441402 [47] WPIDS
DNC C2001-133267
TI Drug delivery system for controlled release of active agent in gastro-intestinal tract comprises a matrix consisting of (non)degradable **polymer**, (non)continuous **membrane** and drug.
DC A96 B07
IN FRIEDMAN, M; **HOFFMAN, A**; KLAUSNER, E; LAVY, E
PA (YISS) YISSUM RES DEV CO HEBREW UNIV JERUSALEM
CYC 94
PI WO 2001037812 A2 20010531 (200147)* EN 46p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001016477 A 20010604 (200153)

ADT WO 2001037812 A2 WO 2000-IL774 20001120; AU 2001016477 A AU 2001-16477 20001120

FDT AU 2001016477 A Based on WO 200137812

PRAI IL 1999-133196 19991129

AB WO 200137812 A UPAB: 20010822

NOVELTY - A gastro-retentive drug delivery system for the controlled release of an active agent in the gastrointestinal (GI) tract comprises a single or multi-layered matrix having a 2D or 3D configuration comprising a **polymer** that retains in the stomach more than a conventional dosage form, a continuous or non-continuous **membrane** and a drug that may be particulate or contained in a drug-containing form.

DETAILED DESCRIPTION - A pharmaceutical gastro-retentive drug delivery system for the controlled release of an active agent in the GI tract comprises a single or multi-layered matrix having a 2D or 3D configuration comprising a **polymer** that does retain in the stomach more than a conventional dosage form, a continuous or non-continuous **membrane** and a drug that may be particulate or contained in a drug-containing form. The **polymer** of the matrix is a degradable **polymer** of a hydrophilic **polymer** that is not readily soluble in gastric fluids, an enteric **polymer** substantially insoluble at pH less than 5.5 and/or a hydrophobic **polymer**, and/or a degradable **polymer**. The **membrane** does not retain in the stomach more than a conventional dosage form, affixed or attached to the matrix, and is a **polymer** with substantial mechanical strength. The drug component is embedded or entrapped in the matrix or is attached to the delivery system and remains in the stomach for 3-24 hours.

An INDEPENDENT CLAIM is also included for the delivery system in the form of a capsule.

USE - A drug release system for the controlled release of an active agent in the GI tract.

ADVANTAGE - Improved efficiency of treatment by reducing the frequency of administration and the application of single doses for improved patient compliance.

DESCRIPTION OF DRAWING(S) - The controlled release drug delivery system.

Controlled release drug delivery system 1
3D matrix containing the drug 100
Strips (fixed to the sides of the matrix to form a continuous **membrane**) 110
Shielding layer 120
Anti-adhering powder layer 130

Dwg.1/5

L15 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:355468 HCAPLUS

DN 135:2504

TI Size-dependent control of the binding of biotinylated proteins to streptavidin using a **polymer** shield

AU Ding, Zhongil; Fong, Robin B.; Long, Cynthia J.; **Stayton, Patrick S.; Hoffman, Allan S.**

CS Department of Bioengineennng, University of Washington, Seattle, WA, 98195, USA

SO Nature (London, U. K.) (2001), 411(6833), 59-62
CODEN: NATUAS; ISSN: 0028-0836
PB Nature Publishing Group
DT Journal
LA English
AB Many medical and biotechnol. processes rely on controlling and manipulating the mol.-recognition capabilities of proteins. This can be achieved using small mols. capable of competing for protein binding or by changing environmental parameters that affect protein structure and hence binding. An alternative is provided by stimuli-responsive polymers that change reversibly from a water-sol. expanded coil to a water-insol. collapsed globule upon small changes in temp., pH or light intensity: when attached to proteins in the vicinity of their binding sites, they reversibly block and release small ligands. Here we show how this approach can be extended to achieve size-selective binding of large, macromol. ligands. We use the thermally responsive polymer poly(N,N-diethylacrylamide) (PDEAAm), and attach it to the protein streptavidin approx. 20 .ANG. from the binding site for biotinylated proteins. Below the lower crit. soln. temp. of PDEAAm, the polymer is in its extended state and acts as a 'shield' to block the binding of large biotinylated proteins; above this temp., it collapses and exposes the binding site, thereby allowing binding. We find that the degree of shielding depends on both the size of the biotinylated protein and the size of PDEAAm, suggesting that 'smart' polymer shields could be tailored to achieve a wide range of size-dependent ligand discrimination for use in affinity sepns., biosensors and diagnostics technologies.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:406498 BIOSIS
DN PREV200100406498
TI Control of shape and size of vascular smooth muscle cells in vitro by plasma lithography.
AU Goessl, Andreas; Bowen-Pope, Daniel F.; **Hoffman, Allan S. (1)**
CS (1) Department of Bioengineering, University of Washington, Seattle, WA, 98195: hoffman@u.washington.edu USA
SO Journal of Biomedical Materials Research, (October, 2001) Vol. 57, No. 1, pp. 15-24. print.
ISSN: 0021-9304.
DT Article
LA English
SL English
AB The ability to control the shape and size of cells is an important enabling technique for investigating influences of geometrical variables on cell physiology. Herein we present a micropatterning technique ("plasma lithography") that uses photolithography and plasma thin-film polymerization for the fabrication of cell culture substrates with a cell-adhesive pattern on a cell-repellent (non-fouling) background. The micron-level pattern was designed to isolate individual vascular smooth muscle cells (SMC) on areas with a projected area of between 25 and 3600 mum2 in order to later study their response to cytokine stimulation in dependence of the cell size and shape as an indication for the phenotypic state of the cells. Polyethylene terephthalate substrates were first coated with a non-fouling plasma **polymer** of tetraglyme (tetraethylene glycol dimethyl ether). In an organic lift-off process, we then fashioned square- and rectangular-shaped islands of a thin fluorocarbon plasma **polymer** film of apprx12-nm thickness. Electron spectroscopy for chemical analysis and secondary ion mass spectroscopy were used to optimize the deposition conditions and

characterize the resulting **polymers**. Secondary ion mass spectroscopy imaging was used to visualized the spatial distribution of the **polymer** components of the micropatterned surfaces. Rat vascular SMC were seeded onto the patterned substrates in serum-free medium to show that the substrates display the desired properties, and that cell shape can indeed be controlled. For long-term maintenance of these cells, the medium was augmented with 10% calf serum after 24 h in culture, and the medium was exchanged every 3 days. After 2 weeks, the cells were still confined to the areas of the adhesive pattern, and when one or more cells spanned more than one island, they did not attach to the intervening tetraethylene glycol dimethyl ether (tetraglyme) background. Spreading-restricted cells formed a well-ordered actin skeleton, which was most dense along the perimeter of the cells. The shape of the nucleus was also influenced by the pattern geometry. These properties make the patterned substrates suitable for investigating if the phenotypic reversion of SMC can be influenced by controlling the shape and size of SMC in vitro.

L15 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:594116 HCAPLUS
DN 133:325550
TI Bioinspired **polymeric** conjugates for biotechnologies
AU **Stayton, Patrick S.; Hoffman, Allan S.; Murthy, Niren;** Cheung, Charles; Lackey, Chantal; Ding, Zhongli; Shimoboji, Tsuyoshi; Press, Oliver
CS Department of Bioengineering, University of Washington, Seattle, WA, 98195, USA
SO Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.) (2000), 41(2), 1607-1608
CODEN: ACPPAY; ISSN: 0032-3934
PB American Chemical Society, Division of Polymer Chemistry
DT Journal
LA English
AB The authors developed polymeric systems to manipulate intracellular trafficking by enhancing transport across the endosomal membrane. Bioinspired polymeric carriers for cytoplasmic delivery of genes and proteins were designed.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:397371 HCAPLUS
DN 136:147277
TI Measured bioeffects of tone-burst ultrasound in combination with poly(propyl acrylic) acid (PPAA)
AU Porter, Tyrone; Hadley, Maile; Nickerson, Josh; Mourad, Pierre; Crum, Lawrence; **Murthy, Niren; Stayton, Patrick; Hoffman, Allan**
CS Applied Physics Laboratory, Seattle, WA, 98105, USA
SO Proceedings - IEEE Ultrasonics Symposium (2000), (Vol. 2), 1359-1362
CODEN: PIEUEZ; ISSN: 1051-0117
PB Institute of Electrical and Electronics Engineers
DT Journal
LA English
AB In this study, High Intensity Focused Ultrasound (HIFU) is combined with the pH-sensitive cell membrane disrupting polymer PPAA (poly-Pr acrylic acid) at sublethal doses to achieve hemolysis of human erythrocytes and sonoporation of suspended cells. For our studies, a 1 mL sample of cells suspended in phosphate buffered saline (PBS) was simultaneously exposed to 1.1 MHz acoustic tone bursts and PPAA at a temp. of 37.degree.. We vary the pH of the suspension fluid and amt. of PPAA added to assess the

influence of its structural conformation, functionality, and concn. upon measured bioeffects. For hemolysis study, we suspended erythrocytes at a final concn. of 108 cells/mL. Damage to the cell suspension was detd. by measuring the amt. of Hb released using a spectrophotometer. A passive cavitation detection system was utilized to monitor the acoustic emissions from the cell suspension during exposure to ultrasound. In the presence of PPAA, there is a significant increase in cavitation and bioeffects during ultrasound exposure at more acidic pH levels. This polymer/ultrasound synergy is pH independent, unlike the synergy of ultrasound with poly(Et acrylic acid). The levels of cavitation and hemolysis measured from HIFU/PPAA synergy was compared with levels measured from HIFU/Optison synergy to assess the effectiveness of the polymer in an acoustic field.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:208542 HCAPLUS
DN 133:109744
TI pH sensitive **membrane disruptive** PEGylated polycations
AU **Murthy, Niren; Stayton, Patrick S.; Hoffman, Allan S.**
CS Department of Bioengineering, University of Washington, Seattle, WA, 98195, USA
SO Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.) (2000), 41(1), 1010-1011
CODEN: ACPPAY; ISSN: 0032-3934
PB American Chemical Society, Division of Polymer Chemistry
DT Journal
LA English
AB A new method for the synthesis of novel PEGylated pH sensitive membrane-disruptive polycations as potential oligonucleotide delivery vehicles has been presented. The strategy is based on grafting PEG onto a hydrophobic-polycationic backbone through an acid degradable acetal linkage. The acetal linkage used for the PEGylation of Copolymer I had a half life of 15 min at pH 5.4, but at pH 7.4 less than 10% of the acetals were hydrolyzed after 80 min. Copolymer I has a hydrolysis rate suitable for drug delivery purposes. The hydrolysis of the PEG grafts and activation of its membrane disruptive activity occur in less than 20 min at pH 5.0. Copolymer I was membrane disruptive at pH 5.0 but not at pH 7.4. The above copolymers should therefore have applications for the delivery of neg. charged polyanions such as DNA or ODNs to cells.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:334740 HCAPLUS
TI pH-Sensitive **membrane disruptive** PEGylated polycations.
AU **Murthy, Niren; Stayton, Patrick; Hoffman, Allan**
CS Bioengineering, University of Washington, Seattle, WA, 98195, USA
SO Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), POLY-551 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69CLAC
DT Conference; Meeting Abstract
LA English
AB Oligonucleotides (ODNs) complementary to specific mRNAs have shown considerable promise for the treatment of diseases such as cancer and viral infections. However, the clin. use of ODNs has been hindered by the

lack of an effective ODN delivery vehicle. PEGylated polycations have recently been considered as an ODN delivery vehicle. PEGylated polycations form polyelectrolyte complexes (PECs) with ODNs. However, the efficiency of pegylated PECs in delivering ODNs is not optimal because endocytosed pegylated PECs are trafficked and degraded in lysosomes. In this report a novel method is developed for the synthesis of PEGylated hydrophobic polycations which have the PEG groups conjugated to the backbone polycations via acid degradable acetal bonds. Thus the pegylated polymers should lose their PEGs and become hydrophobic and membrane disruptive at the endosomal pHs of 6.0 and below, but should not be membrane disruptive at the plasma pH of 7.4. These novel polymers should be useful for delivery of endocytosed anionic drugs such as ODNs and DNA.

L15 ANSWER 9 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:191375 BIOSIS
DN PREV200000191375
TI Molecular engineering of proteins and **polymers** for targeting and intracellular delivery of therapeutics.
AU **Stayton, Patrick S. (1); Hoffman, Allan S.;** **Murthy, Niren;** Lackey, Chantal; Cheung, Charles; Tan, Philip; Klumb, Lisa A.; Chilkoti, Ashutosh; Wilbur, F. Scott; Press, Oliver W.
CS (1) Department of Bioengineering, University of Washington, Seattle, WA, 98195 USA
SO Journal of Controlled Release, (March 1, 2000) Vol. 65, No. 1-2, pp. 203-220.
ISSN: 0168-3659.
DT General Review
LA English
SL English
AB There are many protein and DNA based therapeutics under development in the biotechnology and pharmaceutical industries. Key delivery challenges remain before many of these biomolecular therapeutics reach the clinic. Two important barriers are the effective targeting of drugs to specific tissues and cells and the subsequent intracellular delivery to appropriate cellular compartments. In this review, we summarize protein engineering work aimed at improving the stability and refolding efficiency of antibody fragments used in targeting, and at constructing new streptavidin variants which may offer improved performance in pre-targeting delivery strategies. In addition, we review recent work with pH-responsive **polymers** that mimic the **membrane disruptive** properties of viruses and toxins. These **polymers** could serve as alternatives to fusogenic peptides in gene therapy formulations and to enhance the intracellular delivery of protein therapeutics that function in the cytoplasm.

L15 ANSWER 10 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:533806 BIOSIS
DN PREV200000533806
TI Characterization and gene therapy applications of pH-responsive, **membrane**-active **polymers**.
AU Black, F. E. (1); Cheung, C. Y. (1); **Murthy, N. (1);** **Hoffman, A. S. (1); Stayton, P. S. (1)**
CS (1) Department of Bioengineering, University of Washington, Seattle, WA, 98195 USA
SO Journal of Pharmacy and Pharmacology, (September, 2000) Vol. 52, No. Supplement, pp. 42. print.
Meeting Info.: 137th British Pharmaceutical Conference Birmingham, England, UK September 10-13, 2000
ISSN: 0022-3573.
DT Conference

LA English
SL English

L15 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
AN 1999:451212 HCAPLUS
DN 131:106813
TI Enhanced **transport** using **membrane disruptive** agents
IN **Hoffman, Allan S.**; **Stayton, Patrick**; Press, Oliver; Tirrell, David; **Murthy, Niren**; Lackey, Chantal; Crum, Lawrence A.; Mourad, Pierre D.; Porter, Tyrone M.
PA University of Washington, USA; University of Massachusetts
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9934831	A1	19990715	WO 1999-US122	19990105
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9920261	A1	19990726	AU 1999-20261	19990105
	EP 1044021	A1	20001018	EP 1999-900750	19990105
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 2001007666	A1	20010712	US 1999-226044	19990105
	JP 2002500201	T2	20020108	JP 2000-527278	19990105
PRAI	US 1998-70411	P	19980105		
	WO 1999-US122	W	19990105		

AB Compns. and methods for transport or release of therapeutic and diagnostic agents or metabolites or other analytes from cells, compartments within cells, or through cell layers or barriers are described. The compns. include a membrane barrier transport enhancing agent and are usually administered in combination with an enhancer and/or exposure to stimuli to effect disruption or altered permeability, transport or release. In a preferred embodiment, the compns. include compds. which disrupt endosomal membranes in response to the low pH in the endosomes but which are relatively inactive toward cell membranes, coupled directly or indirectly to a therapeutic or diagnostic agent. Other disruptive agents can also be used, responsive to stimuli and/or enhancers other than pH, such as light, elec. stimuli, electromagnetic stimuli, ultrasound, temp., or combinations thereof. The compds. can be coupled by ionic, covalent or H bonds to an agent to be delivered or to a ligand which forms a complex with the agent to be delivered. Agents to be delivered can be therapeutic and/or diagnostic agents. Treatments which enhance delivery such as ultrasound, iontophoresis, and/or electrophoresis can also be used with the disrupting agents. The ability of the GALA peptide to lyse erythrocytes was compared with that of an GALA/poly(acrylic acid) conjugate at pH 5.0. The conjugate gave 70% lysis at 100 .mu.g.
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:780354 HCAPLUS
DN 132:10527
TI Interactive molecular conjugates
IN **Hoffman, Allan S.**; **Stayton, Patrick S.**
PA University of Washington, USA

SO U.S., 32 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5998588	A	19991207	US 1996-697904	19960830

AB The combination of the capabilities of stimuli-responsive components such as polymers and interactive mols. to form site-specific conjugates which are useful in a variety of assays, sepns., processing, and other uses is disclosed. The polymer chain conformation and vol. can be manipulated through alteration in pH, temp., light, or other stimuli. The interactive mols. can be biomols. like proteins or peptides, such as antibodies, receptors, or enzymes, polysaccharides or glycoproteins which specifically bind to ligands, or nucleic acids such as antisense, ribozymes, and aptamers, or ligands for org. or inorg. mols. in the environment or manufg. processes. The stimuli-responsive polymers are coupled to the recognition biomols. at a specific site so that the polymer can be manipulated by stimulation to alter ligand-biomol. binding at an adjacent binding site, for example, the biotin binding site of streptavidin, the antigen-binding site of an antibody or the active, substrate-binding site of an enzyme. Binding may be completely blocked (i.e., the conjugate acts as an on-off switch) or partially blocked (i.e., the conjugate acts as a rheostat to partially block binding or to block binding only of larger ligands). Once a ligand is bound, it may also be ejected from the binding site by stimulating one (or more) conjugated polymers to cause ejection of the ligand and whatever is attached to it. Alternatively, selective partitioning, phase sepn. or pptn. of the polymer-conjugated biomol. can be achieved through exposure of the stimulus-responsive component to an appropriate environmental stimulus.

RE.CNT 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:246745 BIOSIS
DN PREV199900246745
TI Mice that lack the angiogenesis inhibitor, thrombospondin 2, mount an altered foreign body reaction characterized by increased vascularity.
AU Kyriakides, Themis R.; Leach, Kathleen J.; **Hoffman, Allan S.**; Ratner, Buddy D.; Bornstein, Paul (1)
CS (1) Department of Biochemistry, University of Washington, Seattle, WA, 98195 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (April 13, 1999) Vol. 96, No. 8, pp. 4449-4454.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB **Disruption** of the thrombospondin 2 gene (Thbs2) in mice results in a complex phenotype characterized chiefly by abnormalities in fibroblasts, connective tissues, and blood vessels. Consideration of this phenotype suggested to us that the foreign body reaction (FBR) might be altered in thrombospondin 2 (TSP2)-null mice. To investigate the participation of TSP2 in the FBR, polydimethylsiloxane (PDMS) and oxidized PDMS (ox-PDMS) disks were implanted in TSP2-null and control mice. Growth of TSP2-null and control skin fibroblasts in vitro also was evaluated on both types of disks. Normal fibroblasts grew as a monolayer on both surfaces, but attachment of the cells to ox-PDMS was weak and sensitive to movement. TSP2-null fibroblasts grew as aggregates on both surfaces, and

their attachment was further compromised on ox-PDMS. After a 4-week implantation period, both types of PDMS elicited a similar FBR with a collagenous capsule in both TSP2-null and control mice. However, strikingly, the collagenous capsule that formed in TSP2-null mice was highly vascularized and thicker than that formed in normal mice. In addition, abnormally shaped collagen fibers were observed in capsules from mutant mice. These observations indicate that the presence or absence of an extracellular matrix component, TSP2, can influence the nature of the FBR, in particular its vascularity. The expression of TSP2 therefore could represent a molecular target for local inhibitory measures when vascularization of the tissue surrounding an implanted device is desired.

L15 ANSWER 14 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:281611 BIOSIS
DN PREV199900281611
TI Hemolytic activity of pH-responsive **polymer**-streptavidin bioconjugates.
AU Lackey, Chantal A.; **Murthy, Niren**; Press, Oliver W.; Tirrell, David A.; **Hoffman, Allan S. (1)**; **Stayton, Patrick S.**
CS (1) Department of Bioengineering, University of Washington, Seattle, WA, 98195 USA
SO Bioconjugate Chemistry, (May-June, 1999) Vol. 10, No. 3, pp. 401-405. ISSN: 1043-1802.
DT Article
LA English
SL English
AB Drug delivery systems that increase the rate and/or quantity of drug release to the cytoplasm are needed to enhance cytosolic delivery and to circumvent nonproductive cell trafficking routes. We have previously demonstrated that poly(2-ethylacrylic acid) (PEAAc) has pH-dependent hemolytic properties, and more recently, we have found that poly(2-propylacrylic acid) (PPAAc) displays even greater pH-responsive hemolytic activity than PEAAc at the acidic pHs of the early endosome. Thus, these **polymers** could potentially serve as endosomal releasing agents in immunotoxin therapies. In this paper, we have investigated whether the pH-dependent **membrane disruptive** activity of PPAAc is retained after binding to a protein. We did this by measuring the hemolytic activity of PPAAc-streptavidin model complexes with different protein to **polymer** stoichiometries. Biotin was conjugated to amine-terminated PPAAc, which was subsequently bound to streptavidin by biotin complexation. The ability of these samples to **disrupt** red blood cell **membranes** was investigated for a range of **polymer** concentrations, a range of pH values, and two **polymer** -to-streptavidin ratios of 3:1 and 1:1. The results demonstrate that (a) the PPAAc-streptavidin complex retains the ability to lyse the RBC lipid bilayers at low pHs, such as those existing in endosomes, and (b) the hemolytic ability of the PPAAc-streptavidin complex is similar to that of the free PPAAc.

L15 ANSWER 15 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2000:9745 BIOSIS
DN PREV200000009745
TI The design and synthesis of **polymers** for eukaryotic **membrane disruption.**
AU **Murthy, Niren**; Robichaud, John R.; Tirrell, David A.; **Stayton, Patrick S.**; **Hoffman, Allan S. (1)**
CS (1) Department of Bioengineering, University of Washington, Seattle, WA, 98195 USA

SO Journal of Controlled Release, (Aug. 27, 1999) Vol. 61, No. 1-2, pp. 137-143.
ISSN: 0168-3659.
DT Article
LA English
SL English
AB The intracellular trafficking of drugs is critical to the efficacy of drugs that are susceptible to attack by lysosomal enzymes. It is therefore an important goal to design and synthesize molecules which can enhance the **transport** of endocytosed drugs from the endosomal compartments to the cytoplasm. The pH of an endosome is lower than that of the cytosol by one to two pH units, depending on the stage of endosomal development. This pH gradient is a key factor in the design of **membrane-disruptive polymers** which could enhance the endosomal release of drugs. Such **polymers** should **disrupt** lipid bilayer **membranes** at pH 6.5 and below, but should be non-lytic at pH 7.4. We have designed and synthesized pH-sensitive synthetic **polymers** which efficiently **disrupt** red blood cells within a sharply defined pH range. One of these **polymers**, poly(ethyl acrylic acid) (PEAAc) has been previously shown to **disrupt** synthetic vesicles in a pH-dependent fashion (6). PEAAc hemolyzes red blood cells with an activity of 107 molecules per red blood cell, which is as efficient on a molar basis as the peptide melittin. The mechanism of RBC hemolysis by PEAAc is consistent with the colloid osmotic mechanism. PEAAc's hemolytic activity rises rapidly as the pH decreases from 6.3 to 5.0, and there is no hemolytic activity at pH 7.4. A related **polymer**, poly(propyl acrylic acid) (PPAAc), was synthesized to test whether making the pendant alkyl group more hydrophobic by adding one methylene group would increase the hemolytic activity. PPAAc was found to **disrupt** red blood cells 15 times more efficiently than PEAAc at pH 6.1. PPAAc was also not active at pH 7.4 and displayed a pH-dependent hemolysis that was shifted toward higher pH's. Random 1:1 copolymers of ethyl acrylate (EA) and acrylic acid (AAc) (which contain random -COOH and -C2H5 groups that are present and regularly repeat in PEAAc) also displayed significant hemolytic activity, with an efficiency close to PEAAc. These results demonstrate that pH-sensitive synthetic **polymers** can be molecularly engineered to efficiently **disrupt** eukaryotic **membranes** within defined and narrow pH ranges. Thus, these **polymers** might serve as endosomal **disruptive** agents with specificities for early or late endosomes.

L15 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:481771 HCAPLUS
DN 129:221141
TI Design of **polymers** to increase the efficiency of endosomal release of drugs
AU **Murthy, N.**; Robichaud, J.; **Stayton, P. S.**; Press, O. W.; **Hoffman, A. S.**; Tirrell, D. A.
CS Departments of Bioengineering and Medicine, University of Washington, Seattle, WA, USA
SO Proc. Int. Symp. Controlled Release Bioact. Mater. (1998), 25th, 224-225
CODEN: PCRMEY; ISSN: 1022-0178
PB Controlled Release Society, Inc.
DT Journal
LA English
AB The authors prepd. and investigated the ability of 4 pH-sensitive acrylic polymers to disrupt lipid bilayer membranes by measuring their ability to hemolyze red blood cells. The potential drug delivery polymers were poly(ethacrylic acid), poly(2-propylacrylic acid). poly(2-butylacrylic acid), and acrylic acid-ethacrylic acid copolymer.

L15 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:481705 HCAPLUS
DN 129:235484
TI Stimuli-responsive biomolecular conjugates: controlled **membrane disruption**
AU Lackey, C. A.; **Murthy, N.**; **Stayton, P. S.**; Press, O. W.; **Hoffman, A. S.**; Tirrell, D. A.
CS Departments of Bioengineering and Medicine, University of Washington, Seattle, WA, USA
SO Proc. Int. Symp. Controlled Release Bioact. Mater. (1998), 25th, 87-88
CODEN: PCRMEY; ISSN: 1022-0178
PB Controlled Release Society, Inc.
DT Journal
LA English
AB Poly(ethylacrylic acid) complexed to a protein retains its ability to lyse lipid bilayers at low pH's, such as those existing in endosomes. This demonstrates potential to improve proper therapeutic delivery by facilitating endosomal release.

L15 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:274469 HCAPLUS
DN 126:317781
TI Hybrid biomaterials prepared by ozone-induced polymerization. I. Ozonation of microporous polypropylene
AU Gatenholm, P.; Ashida, T.; **Hoffman, A. S.**
CS Dep. Polymer Technology, Chalmers Univ. Technology, Goteborg, S-412 96, Swed.
SO J. Polym. Sci., Part A: Polym. Chem. (1997), 35(8), 1461-1467
CODEN: JPACEC; ISSN: 0887-624X
PB Wiley
DT Journal
LA English
AB Exposure of isotactic polypropylene (PP) to ozone resulted in surface oxidn., as detected by ESCA, and the formation of peroxides and hydroperoxides. The amt. of oxygen-bearing moieties, as detected by FT-IR, was increased when a microporous membrane with a large surface area was used. Ozonation for an extended period of time, 1-2 h, resulted in a degrdn. of microporous PP, obsd. with SEM as an enlargement of pores and brittle characteristics of the material. The mol. wt. of PP was dramatically reduced after as little as 5 min of ozonation. Exposure to ozone for longer periods of time contributed to further redns. of the mol. wt. and gradual modification of the chem. compn. of PP, restricted, however, to the surface or intercryst. amorphous regions. It was possible to graft 2-hydroxyethyl methacrylate to the ozonated samples, such that the graft copolymer acted as a continuous matrix consequently linked to and reinforced by the PP crystals.

L15 ANSWER 19 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:293762 BIOSIS
DN PREV199598308062
TI Platelet and monoclonal antibody binding to fibrinogen adsorbed on glow-discharge-deposited **polymers**.
AU Kiaei, David; **Hoffman, Allan S. (1)**; Horbett, Thomas A.; Lew, Ken R.
CS (1) Cent. Bioengineering, FL-20, University Washington, Seattle, WA 98195 USA
SO Journal of Biomedical Materials Research, (1995) Vol. 29, No. 6, pp. 729-739.
ISSN: 0021-9304.

DT Article
LA English
AB The state of fibrinogen adsorbed on untreated and glow-discharge-treated surfaces was examined by measuring platelet adhesion, monoclonal antibody (mAb) binding, the amount of fibrinogen adsorbed, and the amount of adsorbed fibrinogen which could be eluted with sodium dodecyl sulfate (SDS). Tetrafluoroethylene (TFE) glow-discharge-treated **polymers** have a lower surface free energy (in air) and retain a larger fraction of adsorbed fibrinogen than untreated surfaces after SDS elution. Platelet adhesion was lowest on the TFE-treated surfaces which retain the highest amounts of fibrinogen after SDS elution. Fibrinogen may undergo unfolding or spreading on the TFE-treated surfaces to minimize interfacial free energy (in water) and maximize protein-surface interactions. When it is adsorbed on the TFE-treated surfaces, fibrinogen evidently assumes a state which somehow prevents its recognition and binding by platelet receptors. Monoclonal antibodies that bind to the three regions in fibrinogen thought to be involved in platelet adhesion were therefore used to detect changes in adsorbed fibrinogen. These regions and the antibodies which bind to them are: the COOH-terminal of the gamma-chain, mAb M1; the RGD peptide sequence at A-alpha 95-98, mAb R1; the RGD sequence at Aa 572-575, mAb R2. For fibrinogen adsorbed on the untreated or TFE-treated surfaces, M1 and R2 binding was relatively high compared to background, while R1 binding was low. However, the amount of binding of each mAb to fibrinogen adsorbed on the TFE-treated surfaces was equal to or greater than fibrinogen adsorbed to the untreated surfaces. Therefore, antibody-detectable changes in the platelet binding regions of adsorbed fibrinogen that might have been caused by conformational or orientational rearrangements were not observed for the TFE-treated surfaces. The data suggest that the tight binding of fibrinogen on a surface may directly affect the ability of the fibrinogen to interact with the platelet receptors-i.e., that fibrinogen must be loosely held to facilitate maximal interaction with platelet receptors.

L15 ANSWER 20 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:403291 BIOSIS
DN PREV199598417591
TI Silicone-based microcarriers: Preparation and BHK cell culture.
AU Denkbas, Emir B.; **Hoffman, Allan S.**; Piskin, Erhan (1)
CS (1) Hacettepe Univ., Chem. Engineering Dep., Bioengineering Div., Ankara Turkey
SO Chemical Engineering Journal, (1995) Vol. 58, No. 1, pp. 65-70.
ISSN: 0923-0467.
DT Article
LA English

L15 ANSWER 21 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 1994:271759 BIOSIS
DN PREV199497284759
TI Activated, N-substituted acrylamide **polymers** for antibody coupling: Application to a novel **membrane**-based immunoassay.
AU Monji, Nobuo (1); Cole, Carol-Ann; **Hoffman, Allan S.**
CS (1) Genet. Systems Corp., 6565 185th Avenue NE, Redmond, WA 98052 USA
SO Journal of Biomaterials Science Polymer Edition, (1994) Vol. 5, No. 5, pp. 407-420.
ISSN: 0920-5063.
DT Article
LA English
AB A room-temperature-precipitable, activated terpolymer consisting of N-isopropylacrylamide (NIPAAm)/N-n-butylacrylamide(nBAAm)/N-

acryloxysuccinimide(NASI) (LCST = 7-13 degree C) at a monomer feed ratio of 60:40:2.5, respectively, was prepared and conjugated to an antibody. The conjugate was evaluated in a novel cellulose acetate (CA) **membrane**-based immunoassay which utilizes the especially strong physical attachment of the **polymer** to CA to bind and concentrate the **polymer** attached protein onto the **membrane**. When compared in the CA **membrane** immunoassay to the antibody-poly(NIPAAm) conjugate prepared via anhydrous copolymerization of NIPAAm and NASI at the monomer feed ratio of 40: 1, respectively, the performance of the NIPAAm/nBAAm/NASI terpolymer was superior to that of the NIPAAm/NASI copolymer (LCST = 32 degree C) when the studies were carried out at room temperature. However, the terpolymer and copolymer gave equivalent performance when the assay mixture was heated to 45 degree C. These results indicate the importance of the LCST of the **polymer** component of the Ab-**polymer** conjugate to its adsorption and binding on the CA **membrane**.

L15 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:651570 HCAPLUS
DN 119:251570
TI Novel biomaterials prepared by ozone-induced polymerization
AU Gatenholm, P.; Ashida, T.; Nabeshima, Y.; **Hoffman, A. S.**
CS Cent. Bioeng., Univ. Washington, Seattle, WA, 98195, USA
SO Polym. Mater. Sci. Eng. (1992), 66, 445-6
CODEN: PMSEDG; ISSN: 0743-0515
DT Journal
LA English
AB The O3-induced graft polymn. of hydroxyethyl methacrylate or N-isopropylacrylamide onto the polypropylene films and microporous membranes was carried out to prep. membrane hydrogel hybrid materials for the immobilization of biolog. active species.

L15 ANSWER 23 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:70604 BIOSIS
DN PREV199395035104
TI Tight binding of albumin to glow discharge treated **polymers**.
AU Kiaei, David; **Hoffman, Allan S.**; Horbett, Thomas A.
CS Cent. Bioengineering, Dep. Chemical Engineering, Univ. Washington, Seattle, Washington 98195 USA
SO Journal of Biomaterials Science Polymer Edition, (1992) Vol. 4, No. 1, pp. 35-44.
ISSN: 0920-5063.
DT Article
LA English
AB Tetrafluoroethylene (TFE) glow discharge-treated Dacron vascular grafts resist thrombus deposition, embolization and thrombotic occlusion. In addition, albumin adsorbed on TFE-treated surfaces resists elution by sodium dodecyl sulfate (SDS). Since the tight binding of albumin to TFE-treated surfaces may contribute to their thromboresistant character, we decided to examine the mechanism responsible for this tenacious adsorption. We have investigated albumin adsorption and retention (after SDS elution) on a number of untreated and glow discharge-treated surfaces. Fluorocarbon glow discharge-treated **polymers** retain a larger fraction of the adsorbed albumin than ethylene and hexamethyldisiloxane glow discharge-treated surfaces. Albumin retention by surfaces appears to be closely related to their surface free energy (in air). Low energy surfaces (in air), whether untreated or glow discharge-treated, retain a larger fraction of the albumin adsorbed than higher energy surfaces. The lowest energy surfaces should have the highest interfacial energies in water, with correspondingly high driving forces for adsorption of

proteins. This can lead to the formation of multiple binding sites upon adsorption, permitting strong hydrophobic interactions, which lead to the observed strong binding.

L15 ANSWER 24 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1991:27062 BIOSIS
DN BA91:16413
TI APPLICATION OF A THERMALLY-REVERSIBLE **POLYMER**-ANTIBODY CONJUGATE IN A NOVEL **MEMBRANE**-BASED IMMUNOASSAY.
AU MONJI N; COLE C-A; TAM M; GOLDSTEIN L; NOWINSKI R C; **HOFFMAN A S**
CS GENETIC SYSTEMS CORP., 3005 FIRST AVE., SEATTLE, WASHINGTON 98121.
SO BIOCHEM BIOPHYS RES COMMUN, (1990) 172 (2), 652-660.
CODEN: BBRCA9. ISSN: 0006-291X.
FS BA; OLD
LA English
AB We have developed a novel method to immobilize antibodies onto a cellulose acetate **membrane** using a conjugate of an N-isopropylacylamid **polymer** covalently bound to the antibody. When compared with the unconjugated antibody, over 30-fold increase in retention of the antibody on the **membrane** was observed when it was conjugated to poly (N-isopropylacrylamide). Studies of the **polymer-membrane** interaction suggest a combination of hydrophobic and ionic forces, especially the former, is responsible for the high retention. We applied this novel immobilization technology in the development of a **membrane**-based immunoassay.

L15 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1989:4185 HCAPLUS
DN 110:4185
TI Polymerization-induced separation assay using recognition pairs
IN Thomas, Elaine K.; Schwartz, Dennis E.; Priest, John H.; Nowinski, Robert C.; **Hoffman, Allan S.**
PA Genetic Systems Corp., USA
SO U.S., 43 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4749647	A	19880607	US 1984-623838	19840622

AB Methods and compds. are disclosed for detg. the presence, amt. of, or assocn. between substances of interest in samples suspected of contg. same. The methods are based on the polymn.-induced sepn. of specifically bound, reporter-labeled recognition reactants from free, reporter-labeled recognition reactants. The methods described are applicable to any substance for which suitable recognition reactants exist or can be made (e.g. antigen/antibody, hormone/receptor, drug/receptor, nucleic acids, chelating agent/ion, etc.) and are not limited by considerations such as chem. compn. or mol. size. Acrylic acid monomer was conjugated to mouse monoclonal antibody to human IgM .kappa. chains via a spacer arm of p-aminobenzoic acid and a 2nd monoclonal antibody to human IgM .mu. chains was labeled with FITC. A simultaneous sandwich immunoassay for human IgM involved incubating the antibodies with sample, copolymg. with 2-hydroxyethyl methacrylate [initiated with TEMED and (NH4)2S2O8], and analyzing by flow cytometry. The fluorescence intensity of copolymer particles formed in the presence of IgM increased 300-fold over control. The increase in intensity was a linear function of the amt. of IgM present in the sample.

L15 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1970:438391 HCAPLUS
DN 73:38391
TI Crosslinked poly(hydroxyethyl methacrylate) **membranes** for desalination by reverse osmosis
AU Jadwin, T. A.; **Hoffman, Allan Sachs**; Vieth, W. R.
CS Dep. of Chem. Eng., Massachusetts Inst. of Technol., Cambridge, Mass., USA
SO J. Appl. Polym. Sci. (1970), 14(5), 1339-59
CODEN: JAPNAB
DT Journal
LA English
AB Crosslinked poly(hydroxyethyl methacrylate) membranes for reverse osmosis desalination were prepd. by adding trimethylolpropane trimethacrylate (I) or ethylene glycol dimethacrylate to thin film homopolymers. Reverse osmosis, osmosis, and sorption tests were performed. The reverse osmosis H2O flux (at 1500 psi applied pressure and 4% NaCl at pH = 5) of the membranes decreased from 0.6 to 0.055 gal/mils/ft2 day, and the salt rejection increased from 78 to 94% max. as the I concn. increased (0-11 mole %). The H2O content decreased from 42 to 15% over the same I range, but the preferential sorption of H2O to salt did not vary. Rises in reverse-osmosis semipermeability were caused by H2O-NaCl diffusivity ratio changes. A mechanism of permselectivity, in terms of parallel diffusive fluxes across the membrane of primary H-bonded H2O and secondary H2O plus salt ions, is discussed.

L15 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1970:122509 HCAPLUS
DN 72:122509
TI Polyacrylic desalination **membranes**. II. Reverse osmosis performance
AU **Hoffman, Allan Sachs**; Modell, Michael; Pan, Peter
CS Dep. of Chem. Eng., Massachusetts Inst. of Technol., Cambridge, Mass., USA
SO J. Appl. Polym. Sci. (1970), 14(2), 285-301
CODEN: JAPNAB
DT Journal
LA English
AB A new class of polyacrylic membranes was tested under reverse osmosis cond itions on dil. (1-4%) salt solns. Fluxes up to 0.2 gal-mil/ft2-day at >98% rejection have been achieved. The effect of membrane compn. on product flux and salt rejection is discus sed. Increased fluxes at even higher rejection should be possible by proper sel ection of the type and concn. of hydrophilic, hydrophobic, and crosslinkin g monomers. Membranes should have as high as possible a concn. of hydrophilic groups, distributed randomly through a lightly crosslinked, rubbery polymer matrix.

L15 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1969:528543 HCAPLUS
DN 71:128543
TI Polyacrylic desalination **membranes**. I. Synthesis and characterization
AU **Hoffman, Allan Sachs**; Modell, Michael; Pan, Peter
CS Massachusetts Inst. of Technol., Cambridge, Mass., USA
SO J. Appl. Polym. Sci. (1969), 13, 2223-34
CODEN: JAPNAB
DT Journal
LA English
AB Polymn. of a mixt. of hydrophilic monomers (N-methylolacrylamide and CH2:CHCO2H), a hydrophobic monomer (CH2:-CHCO2Et), and a hydrophobic

crosslinking monomer (trimethylolpropane trimethacrylate), followed by heat treatment yielded new homogeneous desalination membranes .apprx.6 mils thick. They were characterized by measuring H2O contents and salt distribution coeffs. using an immersion technique. The fractional H2O content in the membrane was 0.16-0.44 with respect to the molal salt distribution coeffs. .apprx.0.22-0.43. A model of intrapolymer H2O is presented: primary H2O is H-bonded with a hydrophilic polymer group while secondary H2O is imbibed with NaCl from the external soln. into hydrophilic regions or defects within the polymer matrix. All compns. contained .apprx.2-3 moles primary H2O/mole hydrophilic monomer. By varying the membrane compn. the sorption characteristics are controlled and can lead to control of flux and permselectivity.

L15 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1969:461922 HCAPLUS
DN 71:61922
TI Structure-property relations for liquid **transport** in modified polypropylene **membranes**
AU Michaels, Alan S.; Vieth, Wolf R.; **Hoffman, Allan Sachs**; Alcalay, Haim A.
CS Massachusetts Inst. of Technol., Cambridge, Mass., USA
SO J. Appl. Polym. Sci. (1969), 13, 577-98
CODEN: JAPNAB
DT Journal
LA English
AB The permeation and permselective properties of polypropylene (I) films towards org. liqs. and vapors were examd. using films subjected to solvent and thermal treatments. The effect of the treatments on film morphology and transport properties was also detd. and structure-property relations for membrane permeation were developed. I film (Profax 6520F) with 95% isotacticity and a mol. wt. of 3 .times. 105 was extruded onto a casting roll at 100.degree. as a polymer melt to give unoriented hot-cast 5-mil thick films used in the expts. Unoriented quenched films prepd. on a casting roll at 20.degree. were also used. The solvents used were isooctane, methylcyclohexane, PhMe, p-xylene, and o-xylene with soly. parameter differences with respect to I of 1, 0.3, 0.8, 0.6, and 0.9 resp. The I film was solvent modified by immersion in solvent baths at 60-100.degree. for 24 hrs. and samples were dried in vacuo at 40.degree.. Liq. permeation fluxes were detd. using a permeation cell in a thermostatted air bath to prevent concn. of the permeant. A normalized flux rate was calcd. The kinetics of vapor sorption were detd. using a quartz-spring balance at const. temp. by admitting a vapor to the evacuated sorption column at satd. vapor pressure and detg. the spring displacement. Film sample d. was detd. using iso-PrOH-H2O d. gradient columns and used to calc. amorphous vol. fraction. Optical and electron microscope examn. were carried out and melt behavior was observed on a differential scanning calorimeter. The measurements were used to det. permeation, sorption, diffusion, and selectivity in treated and untreated films, the effects of permeation temp. and solvent treatments, and the time dependent vapor transport in I. I films were selective towards PhMe relative to isooctane and p-xylene relative to o-xylene. Liq. flux rates depended on the soly. of the permeant in the films, and the abs. difference in the soly. parameters of the polymer-liq. pair provided a good basis for correlation of this effect. In liqs. with similar soly. parameters, fluxes depended on the apparent mol. cross-section of the permeants. Annealed films showed enhanced permeability but reduced selectivity. These effects resulted from the influence of the solvent type on the polymer morphology and the formation of opened spherulitic structures as a result of recrystn. in the presence of the solvent during annealing. Enhanced flux rates resulted from changes in the spherulite

textures and diminished intercryst. tie chain constrainment within the spherulitic substructure.

L15 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1969:58483 HCAPLUS
DN 70:58483
TI Development of ultrathin skin **membranes**-hema **polymers**
AU **Hoffman, Allan S.**; Modell, Michael; Hunter, Jack A.; Gillam, W. Sherman; Podall, Harold E.
CS Massachusetts Inst. of Technol., Cambridge, Mass., USA
SO U. S. Office Saline Water, Res. Develop. Progr. Rep. (1968), No. 374, 30 pp. Avail.: GPO, 55 cents
CODEN: XISWAP
DT Report
LA English
AB A membrane is prepd. by treating a mixt. of acrylic acid 22.7, N-methylolacrylamide 12.3, Et acrylate 40.9, trimethylolpropane trimethacrylate (I) 13.6, and H2O 10.5 vols. with 1% Bz2O2 and a small amt. (2 drops/5 ml. of soln.) of PhNMe2, shaking the compn. for a few sec., pouring it onto Teflon, covering it with glass for 5 min., removing the glass contg. the adherent film, heating the film at 80.degree. for 20 min., and immersing the glass in H2O to release the film, which was 6-8 mils thick and had good mech. properties. This membrane gave slightly better water desalination than did a dense cellulose acetate (39.8% acetylated) membrane. Other membranes prepd. as described above but with smaller amts. of Et acrylate, with no I, or with acrylamide in place of Et acrylate gave less satisfactory desalination. The theory that predicted that the membrane prepd. as described above would be useful in water desalination is discussed.

L15 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1970:512832 HCAPLUS
DN 73:112832
TI Expanded glassy **polymers** and polyelectrolyte complexes as reverse osmosis and ion-selective **membranes**
AU Baddour, Raymond F.; Vieth, Wolf R.; Douglas, Allan S.; **Hoffman, Allan S.**
CS Office of Saline Water, Washington, D. C., USA
SO U.S. Clearinghouse Fed. Sci. Tech. Inform., PB Rep. (1967), No. 191232, 82 pp. Avail.: CFSTI
From: U.S. Govt. Res. Develop. Rep. 1970, 70(13), 80
CODEN: XCCRAO
DT Report
LA English
AB The results of the investigation showed that by varying the membrane prepn. conditions it is possible to control the permeability of the film to dissolved salts. For a given material, however, redn. of the salt permeability usually coincides with redn. of the water flux through the membrane. Many of the materials studied in this investigation show very high salt rejection. For example, cellulose nitrate and hydroxyethyl methacrylate (HEMA) both show salt rejections in excess of 90% at low flow rates, while polyurethanes are just below that value for salt rejection. For each of these 3 materials new techniques were developed to control the water flux and salt rejections, and the technology is now available to control the properties of a variety of hydrophilic polymers. The most promising materials for use in reverse osmosis developed on this program appear to be polyurethanes and HEMA. Both of these, however, still must be prepd. as ultrathin films. Other significant results of this investigation have been the development of new characterization techniques to more fully describe polymer properties and to predict performance.

L15 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2002 ACS
AN 1968:459874 HCAPLUS
DN 69:59874
TI Expanded glassy **polymers** and polyelectrolyte complexes as reverse-osmosis and ion-selective **membranes**
AU Baddour, Raymond F.; Vieth, Wolf R.; Douglas, Allan S.; **Hoffman, Allan S.**; Hunter, J. A.; Gillam, W. Sherman; Podall, H. E.
CS Massachusetts Inst. Technol., Cambridge, Mass., USA
SO U. S. Dep. Interior, Office Saline Water Res. Develop. Progr. Rep. (1967), No. 274, 79 pp. Avail.: GPO, 45 cents
CODEN: XISWAP
DT Report
LA English
AB Various classes of semipermeable membranes were tested in programs for developing new materials with higher water permeabilities and longer useful lifetimes than cellulose acetate, while retaining the salt rejection capacity of the latter polymer. Polyurethanes prepd. from tolylene diisocyanates and polyethylene glycol and cross-linked with trimethylolpropane were studied. The water flux through membranes from this material depended only slightly on chem. crosslink d., but showed a strong dependence on the mol. wt. of the I monomer component. The polyelectrolyte complexes from poly(Na styrenesulfonate) and poly(vinylbenzyltrimethylammonium chloride) showed water flux which varied linearly with the effective pressure. The salt flux through the membrane was linear with respect to osmotic pressure differential, and the normalized salt flux was independent of pressure and upstream salt concn. The transport of both salt and water was about to be primarily diffusive in nature, with the contribution of pore flow or hydrodynamic flow through pin holes being small. Poly(.beta.-hydroxyethyl methacrylate) crosslinked with trimethylolpropane trimethacrylate (II) or ethylene glycol, and methacrylic acid-II-.beta.-hydroxyethyl methacrylate copolymers were also tested. The best results obtained were 94% salt rejection at normalized water-flux 0.1 gallon-mil/ft.2-day for II crosslinked with .apprx.9 mole % III. Salt distribution coeffs. for these membranes were comparable to those in cellulose acetate. A selective annealing method for forming skins on expanded cellulose nitrate films was also developed.

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:58:46 ON 07 MAR 2002
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FILE LAST UPDATED: 5 Mar 2002  (20020305/ED)

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CAS Registry Numbers that were added to the CAS files between 12/27/01
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Numbers with the P indicator executed between 12/27/01 and 1/23/02 may
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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d his


     (FILE 'HOME' ENTERED AT 09:54:09 ON 07 MAR 2002)

     FILE 'HCAPLUS' ENTERED AT 09:54:14 ON 07 MAR 2002
L1          4072 S MEMBRANE? (L) (DISRUPT? OR ALTER?)
L2        988484 S POLYMER##
L3         80442 S CONJUGAT?
L4             4 S L1 AND L2 AND L3
L5            64 S L1 AND L2
L6         33942 S HYDROPHO?
L7         22771 S HYDROPHIL?
L8             1 S L5 AND L6 AND L7
L9         85827 S CELL MEMBRANE/CW
L10           39 S L9 AND L2 AND L3
L11            5 S L10 AND (L6 OR L7)
L12            9 S L5 AND (L6 OR L7)
L13           15 S L4 OR L8 OR L11 OR L12

     FILE 'HCAPLUS' ENTERED AT 09:58:46 ON 07 MAR 2002

=> d .ca 1-15
```

L13 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:638755 HCAPLUS
TITLE: Concentration and removal of endocrine **disruptors** through **hydrophobic polymeric membrane** by pervaporation
AUTHOR(S): Asano, Takao; Yoon, Boo Ok; Hara, Mariko; Higuchi, Akon
CORPORATE SOURCE: Department of Applied Chemistry, Seikei University, Tokyo, 180-8633, Japan
SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), ENVR-176. American Chemical Society: Washington, D. C.
CODEN: 69BUZP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Endocrine disrupting chems., such as dioxin and polychlorinated biphenyl (PCB), are affecting the development and reprodn. of humans and animals, and are, therefore, of major concern to the environment. In this work, we examd. the feasibility of removing endocrine disrupting chems. from extremely dil. aq. solns. through hydrophobic polydimethylsiloxane (PDMS) membranes by pervaporation. 1,2-Dibromo-3-chloropropane (DBCP), diethylphthalate, dioxin and biphenyl were selected as model endocrine disrupting chems. The endocrine disrupting chems. could be sepd. very efficiently from dil. aq. solns. through PDMS membranes by pervaporation when the vacuum line between pervaporation cell and a cold trap on the permeate side was heated to 150 -C. The sepn. factors of the endocrine disrupting chems. could not be correlated well with their mol. size. The hydrophobic endocrine disrupting chems. showed higher sepn. factors than those of hydrophilic endocrine disrupting chems. using hydrophobic PDMS membranes.

L13 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:528152 HCAPLUS
DOCUMENT NUMBER: 135:261910
TITLE: Concentration and removal of endocrine **disruptors** through **hydrophobic polymeric membranes** by pervaporation
AUTHOR(S): Asano, Takao; Yoon, Boo Ok; Hara, Mariko; Higuchi, Akon
CORPORATE SOURCE: Department of Applied Chemistry, Seikei University, Musashino, Tokyo, 180-8633, Japan
SOURCE: Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2001), 41(2), 227-232
CODEN: PEACF2; ISSN: 1524-6434
PUBLISHER: American Chemical Society, Division of Environmental Chemistry
DOCUMENT TYPE: Journal; (computer optical disk)
LANGUAGE: English
AB Endocrine disrupting chems. affect human and animal development and reprodn. and are thus of major environmental concern. The feasibility of removing endocrine disrupting chems. from extremely dil. aq. solns. through hydrophobic polydimethylsiloxane (PDMS) membranes via pervaporation was examd.
CC 61-5 (Water)
ST water purifn pervaporation removal endocrine **disrupting** compd; poldimethylsiloxane **membrane** pervaporation removal endocrine **disrupting** compd
IT Organic compounds, processes

RL: ADV (Adverse effect, including toxicity); PEP (Physical, engineering or chemical process); POL (Pollutant); REM (Removal or disposal); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(endocrine **disrupting**; pervaporation concn. and removal of endocrine **disrupting** compds. through **hydrophobic** polydimethylsiloxane **membranes**)

IT Water purification
(**membrane** sepn.; pervaporation concn. and removal of endocrine **disrupting** compds. through **hydrophobic** polydimethylsiloxane **membranes**)

IT **Membranes**, nonbiological
Water purification
(pervaporation; pervaporation concn. and removal of endocrine **disrupting** compds. through **hydrophobic** polydimethylsiloxane **membranes**)

IT 84-66-2, Diethylphthalate 92-52-4, Biphenyl, processes 96-12-8, 1,2-Dibromo-3-chloropropane 104-51-8, N-Butylbenzene 262-12-4, Dibenzo-p-dioxin 3766-81-2, 2-sec-Butylphenyl methylcarbamate 22781-23-3, 2,2-Dimethyl-1,3-benzodioxol-4-yl methylcarbamate
RL: ADV (Adverse effect, including toxicity); PEP (Physical, engineering or chemical process); POL (Pollutant); REM (Removal or disposal); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(pervaporation concn. and removal of endocrine **disrupting** compds. through **hydrophobic** polydimethylsiloxane **membranes**)

IT 9016-00-6, Polydimethylsiloxane
RL: DEV (Device component use); TEM (Technical or engineered material use); USES (Uses)
(pervaporation **membrane**; pervaporation concn. and removal of endocrine **disrupting** compds. through **hydrophobic** polydimethylsiloxane **membranes**)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:525957 HCAPLUS
DOCUMENT NUMBER: 135:127195
TITLE: Enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**
INVENTOR(S): Hoffman, Allan S.; Stayton, Patrick S.; Murthy, Niren
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051092	A2	20010719	WO 2001-US356	20010105
WO 2001051092	A3	20011206		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-174893 P 20000107

AB Compns. and methods for transport or release of therapeutic and diagnostic agents, metabolites or other analytes from cells, compartments within cells, or through cell layers or barriers are described. The compns. include a membrane barrier transport enhancing agent and are usually administered in combination with an enhancer and/or exposure to stimuli to effect disruption or altered permeability, transport or release. In a preferred embodiment, the compns. include compds. which disrupt endosomal membranes in response to the low pH in the endosomes but which are relatively inactive toward cell membranes (at physiol. pH, but can become active toward cell membranes if the environment is acidified below pH 6.8), coupled directly or indirectly to a therapeutic or diagnostic agent. Other disruptive agents can also be used, responsive to stimuli and/or enhancers other than pH, such as light, elec. stimuli, electromagnetic stimuli, ultrasound, temp., or combinations thereof. The compds. can be coupled by ionic, covalent or H bonds to an agent to be delivered or to a ligand which forms a complex with the agent to be delivered. Agents to be delivered can be therapeutic and/or diagnostic agents. Treatments which enhance delivery such as ultrasound, iontophoresis, and/or electrophoresis can also be used with the disrupting agents. For example, a terpolymer of dimethylaminoethyl methacrylate, Bu methacrylate, and styrene benzaldehyde was prepd. for the membrane-disruptive backbone which was then PEGylated with thiol-terminated monofunctional or heterofunctional PEGs. The acid-degradable linkage was a p-aminobenzaldehyde acetal.

IC ICM A61K047-48

CC 63-6 (Pharmaceuticals)

ST **polymer** cell **membrane disruption** diagnostic therapeutic transport

IT Diagnosis
(agents; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT **Polymers**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates**; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT Animal cell
Cytoplasm
Organelle
(delivery to; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT Amino group
Carboxyl group
Cell **membrane**
Drug targeting
Drugs
Endocytosis
Endosome
Hydroxyl group
Sulfhydryl group
(enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT Antisense oligonucleotides
Biopolymers
Carbohydrates, biological studies

Gene, animal
Nucleotides, biological studies
Oligonucleotides
Peptides, biological studies
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Proteins, general, biological studies
Ribozymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**
)

IT Electric charge
Electromagnetic wave
Electrophoresis
Iontophoresis
Light
Sound and Ultrasound
pH
(enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers** and exposure to stimuli)

IT **Polymer** degradation
(hydrolytic, acid; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT Functional groups
(hydroxyacid; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT Drug delivery systems
(local and systemic; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT Biological transport
(permeation; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT Vinyl compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polymers**; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**)

IT Organic compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**
)

IT Drug delivery systems
(topical; enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**
)

IT 63-42-3DP, Lactose, pyridylthioacetalstyrene-methacrylate **polymer** derivs. with with methoxy-PEG-thiols 554-38-1DP, Hexalysine, pyridylthioacetalstyrene-methacrylate **polymer** derivs. with with methoxy-PEG-thiols 2321-07-5DP, Fluorescein, pyridylthioacetalstyrene-methacrylate **polymer** derivs. with with methoxy-PEG-thiols 134874-49-0DP, fluorescein/hexalysine/lactose derivs. of pyridylthioacetalstyrene-methacrylate **polymers** 282732-40-5DP, reaction products with methoxy-PEG-thiol derivs. of

fluorescein/hexalysine/lactose
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(enhanced transport of therapeutic and diagnostic agents using **membrane disruptive** acid-sensitive **polymers**
)

L13 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:489417 HCAPLUS
DOCUMENT NUMBER: 135:73701
TITLE: Method for the isolation of **hydrophobic** proteins using a phase partition system with an affinity **polymer**
INVENTOR(S): Tjerneld, Folke; Sivars, Ulf
PATENT ASSIGNEE(S): Amersham Pharmacia Biotech AB, Swed.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047947	A2	20010705	WO 2000-EP13025	20001220
WO 2001047947	A3	20011206		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 1999-4803 A 19991227

AB A method for sepg. one or more hydrophobic proteins, for instance membrane proteins such as integral membrane proteins, from a mixt. of proteins is described. The method is characterized in that said mixt. is partitioned in a phase system comprising a micelle-enriched aq. phase (micelle phase) and a polymer-enriched aq. phase (polymer phase). At least part of the polymer of the polymer phase carries an affinity ligand that is capable of binding to an affinity structure on at least one of said one or more hydrophobic proteins. Escherichia coli membranes, contg. genetically-modified cytochrome bo3 ubiquinol oxidase having a histidine tag, were solubilized in a pentaethyleneglycol mono-n-dodecyl ether/dextran T500 two-phase system. The membrane protein phase was removed and washed 3 times with a pure polymer phase before treatment with affinity polymer phase contg. sodium perchlorate and allyldextran T150-IDA-Cu(II) metal chelate.

IC ICM C07K001-00
CC 9-9 (Biochemical Methods)
Section cross-reference(s): 6, 7
ST **hydrophobic** protein sepn phase partition affinity **polymer**; cytochrome bo3 ubiquinol oxidase recombinant membrane purifn; allyldextran IDA copper chelate affinity partition membrane protein
IT Partition
(affinity; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Chelates
RL: BPR (Biological process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(as affinity ligands; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Ligands
RL: BPR (Biological process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates** with **polymers**, binding to **hydrophobic** proteins; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT **Polymers**, biological studies
RL: BPR (Biological process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**, with affinity ligands binding to **hydrophobic** proteins; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Proteins, specific or class
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**hydrophobic**; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Detergents
(ionic; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Proteins, specific or class
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(membrane, integral; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Proteins, specific or class
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(membrane; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Affinity
Buffers
Cell membrane
Ionic strength
Liposomes
Micelles
Partition
Phase
Sample preparation
Temperature
pH
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Proteins, general, analysis

RL: AMX (Analytical matrix); ANST (Analytical study)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT **Polymers**, uses
Salts, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Polyoxyalkylenes, reactions
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); USES (Uses)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Polyoxyalkylenes, biological studies
RL: BPR (Biological process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(reaction with copper(II)iminodiacetic acid; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT Proteins, general, biological studies
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(sepn.; method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT 69671-26-7DP, genetically-modified with C-terminal histidine tag
RL: BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT 9004-54-0D, Dextran T150, allyl derivs., reaction with copper(II)iminodiacetic acid 14219-31-9D, recation with dextran derivs., and PEG
RL: BPR (Biological process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT 25322-68-3DP, PEG, reaction with copper(II)iminodiacetic acid
RL: BPR (Biological process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT 77-86-1, TRIS buffer 110-85-0, Piperazine, uses 151-21-3, Sodium dodecyl sulfate, uses 288-32-4, Imidazole, uses 540-72-7, Sodium isothiocyanate 1119-94-4, Dodecyltrimethylammonium bromide 1132-61-2, MOPS 3055-95-6, Pentaethylene glycol mono-n-dodecyl ether 5704-04-1, Tricine 7365-44-8 7365-45-9, HEPES 7558-79-4, Disodium hydrogen phosphate 7558-80-7, Sodium dihydrogen phosphate 7601-89-0, Sodium perchlorate 7647-14-5, Sodium chloride, uses 7647-15-6, Sodium bromide, uses 9002-93-1, Triton X-100 9004-54-0, Dextran T500, uses 41444-50-2, Octylglucoside 61012-50-8 69227-93-6
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

IT 25322-68-3, PEG
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); USES (Uses)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)
IT 142-73-4, Iminodiacetic acid 7719-09-7, Thionyl chloride 7758-98-7, Copper (II) sulfate, reactions
RL: RCT (Reactant)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)
IT 142-73-4DP, Iminodiacetic acid, reaction products with chlorinated polyoxyethylene 27252-69-3DP, reaction products with iminodiacetic acid 27252-69-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(method for isolation of **hydrophobic** proteins using phase partition systems with affinity **polymers**)

L13 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:310488 HCAPLUS
DOCUMENT NUMBER: 134:331596
TITLE: **Polymer**-lipid **conjugate** for fusion of target membranes
INVENTOR(S): Martin, Francis J.; Zalipsky, Samuel
PATENT ASSIGNEE(S): Sequus Pharmaceuticals, Inc., USA
SOURCE: U.S., 38 pp., Cont.-in-part of U.S. 5,891,468.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6224903	B1	20010501	US 1998-208684	19981210
US 5891468	A	19990406	US 1997-949046	19971010

PRIORITY APPLN. INFO.: US 1996-28269 P 19961011
US 1997-949046 A2 19971010

AB A fusogenic liposome compn. for delivering a liposome-entrapped compd. into the cytoplasm of a target cell is described. The liposomes have an outer surface coating of chem. releasable hydrophilic polymer chains which shield hydrophobic polymers on the liposome outer surface. Release of the hydrophilic polymer chains exposes the hydrophobic polymers for interaction with outer cell membranes of the target cells to promote fusion of the liposome with the target cells. Also disclosed is a polymer-lipid conjugate for use in promoting fusion between target membranes. The conjugate is composed of a first segment composed of a hydrophilic polymer and a second hydrophobic polymer segment. The second segment is joined to the first segment by a bond effective to release the first segment in response to an existing or an induced physiol. condition. Attached to the second segment is a vesicle-forming lipid member.

IC ICM A61K009-127
NCL 424450000
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 35
ST liposome fusogenic **polymer conjugate** lipid targeting
IT Functional groups
(alkoxycarbonyl groups; **polymer**-lipid **conjugate** for fusion of target membranes)
IT Redox potential
(biol.; **polymer**-lipid **conjugate** for fusion of

target membranes)
IT Animal virus
(fusion peptides of; **polymer**-lipid **conjugate** for fusion of target membranes)
IT **Polymers**, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**hydrophilic**; **polymer**-lipid **conjugate** for fusion of target membranes)
IT **Polymers**, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**hydrophobic**; **polymer**-lipid **conjugate** for fusion of target membranes)
IT Erythrocyte
(liposomal fusion with; **polymer**-lipid **conjugate** for fusion of target membranes)
IT Drug delivery systems
(liposomes; **polymer**-lipid **conjugate** for fusion of target membranes)
IT Antitumor agents
Cell membrane
Disulfide group
Drug targeting
Fusion, biological
Genetic vectors
Infection
Inflammation
Membrane, biological
Molecular weight distribution
Neoplasm
(**polymer**-lipid **conjugate** for fusion of target membranes)
IT Polycarbonates, biological studies
Polyoxyalkylenes, biological studies
Polyoxyphenylenes
Polysulfones, biological studies
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymer**-lipid **conjugate** for fusion of target membranes)
IT Enzymes, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(signal sequence cleavage by; **polymer**-lipid **conjugate** for fusion of target membranes)
IT Lipids, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(vesicle-forming; **polymer**-lipid **conjugate** for fusion of target membranes)
IT Peptides, biological studies
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(viral fusion; **polymer**-lipid **conjugate** for fusion of target membranes)
IT 9001-12-1, Collagenase 9004-06-2, Elastase 9004-08-4, Cathepsin 9025-39-2, Heparinase 9040-48-6, Gelatinase 141907-41-7, Matrix

metalloproteinase
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**polymer**-lipid **conjugate** for fusion of target membranes)

IT 285552-08-1, Plglwa peptide+ 335596-40-2, Ffgavigtialgvatsaqitagiala peptide+ 335596-41-3, Fagvviglaalgvataaqvtaavalv peptide+ 335596-42-4, Fagvvlagaalgvataaqitagial peptide+ 335596-43-5, Figaiiggvalgvataaqit peptide+ 335596-44-6, Flgfllgvgsaiasgvavskvlhleg peptide+ 335596-45-7, Avgigamflgflgaagstmgaasmtl peptide+ 335596-46-8, Kftivfphnqkgnwknvpsnyhycps peptide+ 335596-47-9, Kfpiytildklgpwspidihhlscpn peptide+ 335596-48-0, Lfgaiagfiengwegmidgwygfrhq peptide+ 335596-49-1, Ffgaiagfleggwegmiagwhgytsh peptide+ 335596-51-5, Ifgiddliiglllfvaivetgiggyll peptide+
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymer**-lipid **conjugate** for fusion of target membranes)

IT 9002-88-4, Polyethylene 9003-07-0, Polypropylene 9003-53-6, Polystyrene 25190-06-1, Polytetramethylene ether 25322-69-4, Polypropylene oxide
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymer**-lipid **conjugate** for fusion of target membranes)

IT 59-30-3DP, Folic acid, **conjugates** 66-72-8DP, Pyridoxal, **conjugates**
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**polymer**-lipid **conjugate** for fusion of target membranes)

IT 9046-10-0 80506-64-5
RL: RCT (Reactant)
(**polymer**-lipid **conjugate** for fusion of target membranes)

IT 179761-24-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(**polymer**-lipid **conjugate** for fusion of target membranes)

IT 207287-03-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(**polymer**-lipid **conjugate** for fusion of target membranes)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:284998 HCAPLUS
DOCUMENT NUMBER: 133:105858
TITLE: Facilitated transport of organics of biological interest I. A new **alternative** for the separation of amino acids by fixed-site crown-ether polysiloxane **membranes**
AUTHOR(S): Barboiu, M.; Guizard, C.; Hovnanian, N.; Palmeri, J.; Reibel, C.; Cot, L.; Luca, C.
CORPORATE SOURCE: Laboratoire des Materiaux et Procedes Membranaires CNRS UMR 5635, Montpellier, F-34296, Fr.

SOURCE: J. Membr. Sci. (2000), 172(1-2), 91-103
CODEN: JMESDO; ISSN: 0376-7388
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fixed-site heteropolysiloxane membranes contg. grafted macrocyclic receptors can sep. a mixt. of amino acids. These membranes have an intermediate configuration between liq. membranes (selective complexation by a specific carrier) and solid membranes (charge interactions).The soln.-diffusion model, which was used to analyze exptl. transport results for these membranes, provided evidence for a new dual transport mechanisms. With an acidic pH of the feed phase, the selectivity of the transport (symport of protons) relative to l-.alpha.-alanine (Ala) was high and dependent on the relative hydrophobicity of the amino acids (l-Ph aniline (She), leucine (Leu)) (S=7-10), whereas no selectivity was obtained when the pH of the feed phase was higher. The proton-driven transport increased the flux and caused the transport rates of amino acids to be widely spread out due to different mol. recognition principles effecting transport. An active transport mechanism of amino acids is possibly present in the solid dense polymeric matrix.

CC 38-3 (Plastics Fabrication and Uses)
Section cross-reference(s): 34

IT Complexation
Hydrophobicity
Molecular recognition
Permeability
Transport properties
Zwitterions
(**alternative** for sepn. of amino acids by fixed-site crown-ether polysiloxane **membranes**)

IT **Membranes**, nonbiological
(liq.; **alternative** for sepn. of amino acids by fixed-site crown-ether polysiloxane **membranes**)

IT Amino acids, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(neat and in zwitterionic form; **alternative** for sepn. of amino acids by fixed-site crown-ether polysiloxane **membranes**)

IT Polysiloxanes, uses
RL: PRP (Properties); TEM (Technical or engineered material use); USES (Uses)
(poly(ether sulfonate)-supported; **alternative** for sepn. of amino acids by fixed-site crown-ether polysiloxane **membranes**)

IT Polysulfones, uses
RL: NUU (Other use, unclassified); USES (Uses)
(polyether-, **polymeric membranes** supported with; **alternative** for sepn. of amino acids by fixed-site crown-ether polysiloxane **membranes**)

IT Polyethers, uses
RL: NUU (Other use, unclassified); USES (Uses)
(polysulfone-, **polymeric membranes** supported with; **alternative** for sepn. of amino acids by fixed-site crown-ether polysiloxane **membranes**)

IT 56-40-6, Glycine, processes 56-41-7, L-.alpha.-Alanine, processes 56-45-1, L-Serine, processes 56-84-8, Aspartic acid, processes 56-87-1, L-Lysine, processes 61-90-5, L-Leucine, processes 63-91-2, L-Phenyl alanine, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(neat and in zwitterionic form; **alternative** for sepn. of amino acids by fixed-site crown-ether polysiloxane **membranes**)

IT 283614-51-7

RL: PRP (Properties); TEM (Technical or engineered material use); USES (Uses)
(poly(ether sulfonate)-supported; **alternative** for sepn. of amino acids by fixed-site crown-ether polysiloxane **membranes**)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:255871 HCAPLUS
DOCUMENT NUMBER: 133:103745
TITLE: Modulation of immobilized enzyme activity by **altering** the **hydrophobicity** of nylon-grafted **membranes** Part 1. Isothermal conditions
AUTHOR(S): El-Masry, M. M.; De Maio, A.; Di Martino, S.; Diano, N.; Bencivenga, U.; Rossi, S.; Grano, V.; Canciglia, P.; Portaccio, M.; Gaeta, F. S.; Mita, D. G.
CORPORATE SOURCE: International Institute of Genetics and Biophysics of CNR, Naples, 80125, Italy
SOURCE: J. Mol. Catal. B: Enzym. (2000), 9(4-6), 219-230
CODEN: JMCEF8; ISSN: 1381-1177
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The catalytic behavior under isothermal conditions of two different membranes loaded with .beta.-galactosidase was investigated. One membrane (M1) was constituted by a nylon sheet grafted with methylmethacrylate by means of chem. grafting. The other, (M2), was prepd. by a double chem. grafting: the first one with styrene (Sty) and the second one with methylmethacrylate. Membrane activity was characterized as a function of temp., pH and substrate concn. The role of Sty in increasing membrane hydrophobicity has been discussed. Membrane M2 was found to be better suited for employment in non-isothermal bioreactors.

CC 16-1 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 7, 9

IT Immobilization, biochemical
(enzyme; modulation of immobilized enzyme activity under isothermal conditions by **altering** the **hydrophobicity** of nylon-grafted **membranes**)

IT Polyamides, preparation
RL: NUU (Other use, unclassified); PNU (Preparation, unclassified); PREP (Preparation); USES (Uses)
(graft **polymers**; modulation of immobilized enzyme activity under isothermal conditions by **altering** the **hydrophobicity** of nylon-grafted **membranes**)

IT Polyamide fibers, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**membrane** grafted with methylmethacrylate or styrene and methylmethacrylate; modulation of immobilized enzyme activity under isothermal conditions by **altering** the **hydrophobicity** of nylon-grafted **membranes**)

IT Enzyme kinetics
Hydrophobicity
Temperature effects, biological
pH
(modulation of immobilized enzyme activity under isothermal conditions by **altering** the **hydrophobicity** of nylon-grafted **membranes**)

IT 50-99-7P, Dextrose, preparation
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP

(Preparation)
(modulation of immobilized enzyme activity under isothermal conditions by **altering** the **hydrophobicity** of nylon-grafted **membranes**)

IT 9031-11-2, .beta.-Galactosidase
RL: BPR (Biological process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(modulation of immobilized enzyme activity under isothermal conditions by **altering** the **hydrophobicity** of nylon-grafted **membranes**)

IT 63-42-3, Lactose
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(modulation of immobilized enzyme activity under isothermal conditions by **altering** the **hydrophobicity** of nylon-grafted **membranes**)

IT 124-09-4, Hexamethylenediamine, reactions 9003-53-6D, PolyStyrene, grafted copolymer with nylon **membrane** and polymethylmethacrylate 9011-14-7D, PolyMethylmethacrylate, grafted copolymer with nylon **membrane**
RL: NUU (Other use, unclassified); RCT (Reactant); USES (Uses)
(modulation of immobilized enzyme activity under isothermal conditions by **altering** the **hydrophobicity** of nylon-grafted **membranes**)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:451212 HCAPLUS
DOCUMENT NUMBER: 131:106813
TITLE: Enhanced transport using **membrane disruptive** agents
INVENTOR(S): Hoffman, Allan S.; Stayton, Patrick; Press, Oliver; Tirrell, David; Murthy, Niren; Lackey, Chantal; Crum, Lawrence A.; Mourad, Pierre D.; Porter, Tyrone M.
PATENT ASSIGNEE(S): University of Washington, USA; University of Massachusetts
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9934831	A1	19990715	WO 1999-US122	19990105
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9920261	A1	19990726	AU 1999-20261	19990105
EP 1044021	A1	20001018	EP 1999-900750	19990105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2001007666	A1	20010712	US 1999-226044	19990105
JP 2002500201	T2	20020108	JP 2000-527278	19990105

PRIORITY APPLN. INFO.: US 1998-70411 P 19980105
WO 1999-US122 W 19990105

AB Compns. and methods for transport or release of therapeutic and diagnostic agents or metabolites or other analytes from cells, compartments within

cells, or through cell layers or barriers are described. The compns. include a membrane barrier transport enhancing agent and are usually administered in combination with an enhancer and/or exposure to stimuli to effect disruption or altered permeability, transport or release. In a preferred embodiment, the compns. include compds. which disrupt endosomal membranes in response to the low pH in the endosomes but which are relatively inactive toward cell membranes, coupled directly or indirectly to a therapeutic or diagnostic agent. Other disruptive agents can also be used, responsive to stimuli and/or enhancers other than pH, such as light, elec. stimuli, electromagnetic stimuli, ultrasound, temp., or combinations thereof. The compds. can be coupled by ionic, covalent or H bonds to an agent to be delivered or to a ligand which forms a complex with the agent to be delivered. Agents to be delivered can be therapeutic and/or diagnostic agents. Treatments which enhance delivery such as ultrasound, iontophoresis, and/or electrophoresis can also be used with the disrupting agents. The ability of the GALA peptide to lyse erythrocytes was compared with that of an GALA/poly(acrylic acid) conjugate at pH 5.0. The conjugate gave 70% lysis at 100 .mu.g.

IC ICM A61K047-32
ICS A61K047-42; A61K047-48; A61K041-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 37

ST drug transport **membrane disruptive** agent prepn; **polymer** protein **conjugate** drug transport prepn

IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G, **conjugates**, with **polymers**; enhanced drug transport using **membrane disruptive** agents)

IT Biological transport
(drug; enhanced drug transport using **membrane disruptive** agents)

IT Drug delivery systems
(emulsions; enhanced drug transport using **membrane disruptive** agents)

IT Cell **membrane**
Cytotoxic agents
Electric field
Electrophoresis
Endosome
Erythrocyte
Gene therapy
Hemolysis
Iontophoresis
Sound and Ultrasound
(enhanced drug transport using **membrane disruptive** agents)

IT **Polymer** blends
RL: POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced drug transport using **membrane disruptive** agents)

IT Lipids, biological studies
Nucleic acids
Nucleosides, biological studies
Nucleotides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced drug transport using **membrane disruptive** agents)

IT Drug delivery systems
(liposomes; enhanced drug transport using **membrane**

disruptive agents)
IT Drug delivery systems
(microparticles; enhanced drug transport using **membrane disruptive** agents)
IT Drug delivery systems
(nanoparticles; enhanced drug transport using **membrane disruptive** agents)
IT 79-10-7D, Acrylic acid, **polymers** 9003-01-4D, Poly(Acrylic acid), protein **conjugates**
RL: POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced drug transport using **membrane disruptive** agents)
IT 107658-43-5DP, Peptide GALA (synthetic pore-forming), **polymer conjugates**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(enhanced drug transport using **membrane disruptive** agents)
IT 9013-20-1D, Streptavidin, **conjugates** with **polymers**
25119-83-9, Acrylic acid-butyl acrylate copolymer 62607-09-4, Poly(ethacrylic acid) 62607-09-4D, Poly(ethacrylic acid), protein **conjugates** 75034-36-5, Acrylic acid-propyl acrylate copolymer 138134-74-4, Poly(.alpha.-propylacrylic acid) 138134-76-6, Poly(.alpha.-butylacrylic acid)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced drug transport using **membrane disruptive** agents)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:740133 HCAPLUS
DOCUMENT NUMBER: 128:26910
TITLE: Polypeptide **conjugates** for transporting substances across cell membranes
INVENTOR(S): Summerton, James E.; Weller, Dwight D.
PATENT ASSIGNEE(S): Antivirals Inc., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740854	A2	19971106	WO 1997-US7335	19970430
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9729298	A1	19971119	AU 1997-29298	19970430
AU 729643	B2	20010208		
EP 966303	A2	19991229	EP 1997-923513	19970430
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL				

JP 2000509394 T2 20000725 JP 1997-539221 19970430
PRIORITY APPLN. INFO.: US 1996-16347 P 19960501
US 1996-28609 P 19961023
WO 1997-US7335 W 19970430

AB Polymeric compns. effective for delivering compds. in living organisms are described. The compns. include polypeptides which exhibit soly. in both hydrophilic and lipophilic environments by undergoing a reversible pH-dependent transition from a low-pH, lipophilic form to a high-pH, hydrophilic form.

IC ICM A61K047-48

CC 63-5 (Pharmaceuticals)

ST transdermal drug delivery peptide **conjugate** antitumor; antiulcer drug delivery peptide **conjugate**; anticaries drug delivery peptide **conjugate**

IT Proteins (specific proteins and subclasses)
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; polypeptide **conjugates** for transporting substances across cell membranes)

IT Stratum corneum (epidermis)
(extracellular matrix; polypeptide **conjugates** for transporting substances across cell membranes)

IT **Polymers**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleic acid-binding; polypeptide **conjugates** for transporting substances across cell membranes)

IT Nucleic acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**polymers** binding; polypeptide **conjugates** for transporting substances across cell membranes)

IT Antibacterial agents
Antitumor agents
Cell membrane
Dentifrices
Drug delivery systems
Helicobacter pylori
Hydrophilicity
Lipophilicity
Partition
Protein sequences
Transdermal drug delivery systems
.alpha.-Helix (protein conformation)
(polypeptide **conjugates** for transporting substances across cell membranes)

IT 25513-46-6, Polyglutamic acid
RL: BOC (Biological occurrence); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(polypeptide **conjugates** for transporting substances across cell membranes)

IT 1397-89-3D, Amphotericin b, polypeptide **conjugates**
33069-62-4D, Taxol, polypeptide **conjugates** 79217-60-0D, Cyclosporin, polypeptide **conjugates**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polypeptide **conjugates** for transporting substances across cell membranes)

IT 56-41-7, Alanine, biological studies 56-86-0, Glutamic acid, biological studies 61-90-5, Leucine, biological studies 63-68-3, Methionine, biological studies 107-95-9, .beta.-Alanine 2835-81-6, 2-Amino butyric acid 6600-40-4, Norvaline
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);

BIOL (Biological study); OCCU (Occurrence)
(polypeptides contg.; polypeptide **conjugates** for transporting substances across cell membranes)

L13 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:667263 HCAPLUS
DOCUMENT NUMBER: 127:322794
TITLE: Property-affecting and/or property-exhibiting compositions for therapeutic and diagnostic uses
INVENTOR(S): Rabbani, Elazar; Stavrianopoulos, Jannis G.; Donegan, James J.; Liu, Dakai; Kelker, Norman E.; Engelhardt, Dean L.
PATENT ASSIGNEE(S): Enzo Therapeutics, Inc., USA
SOURCE: Can. Pat. Appl., 275 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2190304	AA	19970616	CA 1996-2190304	19961114
EP 779365	A2	19970618	EP 1996-119961	19961212
EP 779365	A3	19991124		
R: DE, FR, GB, IT				
JP 09313190	A2	19971209	JP 1996-360043	19961216
US 2001006814	A1	20010705	US 1997-978633	19971125
US 2001006815	A1	20010705	US 1997-978634	19971125
US 2001006816	A1	20010705	US 1997-978637	19971125
US 2001007767	A1	20010712	US 1997-978632	19971125

PRIORITY APPLN. INFO.: US 1995-574443 A 19951215

AB Compns. useful for effecting and/or exhibiting changes in biol. functioning and processing in cells and biol. systems are provided which combine chem. modifications and/or ligand addns. with biol. functions in such a way as not to interfere substantially with the biol. functions. Such addnl. characteristics include nuclease resistance, targeting specific cells or cell receptors, and augmenting or decreasing interactions between the compns. and target cells. A title compn. may constitute a nucleotide, nucleotide analog, nucleic acid, natural or synthetic polymer, ligand, or conjugate of a ligand with any of the preceding. For example, single-stranded DNA from a plasmid contg. a gene of interest is complexed with an allylamine phosphoramidite-contg. oligonucleotide primer (complementary to a region of the DNA distant from the gene of interest) which as been modified with trilactosyllysyllysine (prepn. given), and the primer is extended with Klenow enzyme to form completely double-stranded DNA. On exposure of target cells to this DNA, the galactose moieties on the DNA bind to receptors on the cells, resulting in transport of the DNA into the cells. In another embodiment, DNA for antisense RNA sequences to regions of the HIV genome were inserted into the U1 small nuclear RNA coding region and the DNA was used to transform U937 cells. The transformed cells were resistant to HIV infection, as shown by inhibition of virus replication and p24 antigen prodn.

IC ICM C07H021-00
ICS A61K047-48; A61K031-70; A61K038-55

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 3

ST polynucleotide **conjugation** ligand cell targeting; protein **conjugation** ligand cell targeting; HIV gene therapy; biopolymer

cell targeting)
IT Bacteria (Eubacteria)
Eukaryote (Eukaryotae)
Prokaryote
(DNA of, **conjugates** with ligands; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Ligands
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugated**, with nucleic acids; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Plasmids
(**conjugates** with ligands; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Biopolymers
Fatty acid esters
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**conjugates** with nucleic acids; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Polyelectrolytes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates** with nucleic acids; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Fatty acids, biological studies
Polymers, biological studies
Proteins (specific proteins and subclasses)
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**conjugates** with nucleic acids; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Bond
Molecules
(**hydrophobic**; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT **Cell membrane**
Cytoplasm
(localization to; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Bacteriophage
Viroid
(nucleic acid of, **conjugates** with ligands; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Animal virus
(nucleic acids of, **conjugates** with ligands; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT Antibody **conjugates**
Monoclonal antibody **conjugates**
Polysaccharide **conjugates**
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(with nucleic acids; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)
IT 9004-10-8DP, Insulin, **conjugates** with oligo(T)
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses)

L13 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:372273 HCAPLUS
DOCUMENT NUMBER: 126:347323
TITLE: Buccal delivery of glucagon-like insulinotropic peptides (GLPs)
INVENTOR(S): Heiber, Sonia J.; Ebert, Charles D.; Gutniak, Mark K.
PATENT ASSIGNEE(S): Theratech, Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715296	A1	19970501	WO 1996-US16890	19961022
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
US 5766620	A	19980616	US 1995-553807	19951023
CA 2235369	AA	19970501	CA 1996-2235369	19961022
AU 9674647	A1	19970515	AU 1996-74647	19961022
AU 716038	B2	20000217		
EP 859606	A1	19980826	EP 1996-936815	19961022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1202820	A	19981223	CN 1996-198618	19961022
BR 9611139	A	19990406	BR 1996-11139	19961022
JP 11513982	T2	19991130	JP 1996-516712	19961022
TW 416854	B	20010101	TW 1996-85112962	19961022
ZA 9608909	A	19970528	ZA 1996-8909	19961023
US 5863555	A	19990126	US 1997-964731	19971105

PRIORITY APPLN. INFO.: US 1995-553807 A 19951023
WO 1996-US16890 W 19961022

AB Drug delivery systems for administering a GLP to the buccal mucosa for transmucosal drug delivery comprise a drug compn. contg. effective amts. of the GLP and a permeation enhancer, and means for maintaining the drug compn. in a drug-transferring relation with the buccal mucosa. These systems can be in free form, such as creams, gels, and ointments, or can comprise a device of detd. phys. form, such as tablets, patches, and troches. A preferred GLP is GLP-1(7-36) amide. Thus, a gingival bilayer tablet was prepd. comprising an active layer and an adhesive layer. The adhesive layer was prepd. by mixing polyethylene oxide 70, Carbopol 934P 20, and compressible xylitol/CM-cellulose filler 10 wt. parts, granulating with EtOH, sieving, drying, mixing with stearic acid 0.25 and mint flavor 0.06 wt.%, and compression. To prep. the active layer, mannitol 49.39, hydroxypropylcellulose 34.33, and Na taurocholate 15.00 wt.% were mixed, granulated with EtOH, sieved, dried, combined with GLP-1(7-36) amide 0.91, FD&C Yellow No. 6HT 0.06, Mg stearate 0.25, and mint flavor 0.06 wt.%; 50 mg of this mixt. was compressed onto 50 mg adhesive layer.

IC ICM A61K009-70
ICS A61L015-16
CC 63-6 (Pharmaceuticals)
IT Caseins, biological studies
Gelatins, biological studies

Polyethers, biological studies
Vinyl **polymers**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adhesives contg.; buccal delivery of glucagon-like insulinotropic peptides)

IT **Cell membrane**
(**disrupting** agents for; buccal delivery of glucagon-like insulinotropic peptides)

IT **Polymers**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hydrophilic**, adhesive contg.; buccal delivery of glucagon-like insulinotropic peptides)

IT 79-10-7D, 2-Propenoic acid, esters, **polymers** 79-10-7D, 2-Propenoic acid, **polymers** 557-75-5D, Ethenol, **polymers** 9000-30-0, Guar gum 9000-69-5, Pectin 9003-39-8, PVP 9004-32-4 9004-54-0, Dextran, biological studies 9004-57-3, Ethylcellulose 9004-62-0, Hydroxyethylcellulose 9004-64-2, Hydroxypropylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9005-25-8, Starch, biological studies 25322-68-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adhesive contg.; buccal delivery of glucagon-like insulinotropic peptides)

IT 107-35-7D, Taurine, bile acid **conjugates**, salts 12441-09-7D, Sorbitan, esters 25312-65-6D, Cholanic acid, salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

L13 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:262361 HCAPLUS
DOCUMENT NUMBER: 116:262361
TITLE: Modified polyanionic **polymers**. I: Grafting of **hydrophobic** group onto poly(maleic acid-alt-3,4-dihydroxyphenylprop-1-ene) to improve the affinity for cell membranes
AUTHOR(S): Suda, Yasuo; Yamamoto, Hitomi; Sumi, Masao; Oku, Naoto; Ito, Fumiaki; Yamashita, Shinji; Nadai, Tanekazu; Ottenbrite, Raphael M.
CORPORATE SOURCE: Fac. Sci., Osaka Univ., Toyonaka, 560, Japan
SOURCE: J. Bioact. Compat. Polym. (1992), 7(1), 15-24
CODEN: JBCPEV; ISSN: 0883-9115
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To improve the affinity of polyanionic polymers for cell membranes, several hydrophobic groups were grafted onto poly(maleic acid-alt-3,4-dihydroxyphenylprop-1-ene) [poly(MA-alt-DP)] which has cytotoxic activity. The effect of the degree of substitution of the grafted group to the maleic anhydride residue was also evaluated. Grafted polymers were characterized by their partition coeffs., their affinity to liposomes and the ability to interact with rat small intestinal epithelial cells. The cell affinity of the modified polyanionic polymers could be augmented and controlled by simple grafting.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 35

ST maleate dihydroxyphenylpropene **polymer** amine graft; cell affinity **polymer**

IT Cell **membrane**
(affinity of amine grafted-diacetoxyphenylpropene-maleic anhydride **alternating** copolymer for)

IT Lipophilicity

(of amine grafted-diacetoxyphenylpropene-maleic anhydride **alternating** copolymers, affinity for cell **membranes** in relation to)

IT Amines, compounds
RL: SPN (Synthetic preparation); PREP (Preparation)
(reaction products, with diacetoxyphenylpropene-maleic anhydride **alternating** copolymer, hydrolyzed, prepn. and affinity for cell **membranes** of)

IT 62-53-3DP, Aniline, reaction products with diacetoxyphenylpropene-maleic anhydride **alternating** copolymer, hydrolyzed 107-10-8DP, Propylamine, reaction products with diacetoxyphenylpropene-maleic anhydride **alternating** copolymer, hydrolyzed 109-73-9DP, Butylamine, reaction products with diacetoxyphenylpropene-maleic anhydride **alternating** copolymer, hydrolyzed 111-26-2DP, Hexylamine, reaction products with diacetoxyphenylpropene-maleic anhydride **alternating** copolymer, hydrolyzed 111-86-4DP, Octylamine, reaction products with diacetoxyphenylpropene-maleic anhydride **alternating** copolymer, hydrolyzed 2016-57-1DP, Decylamine, reaction products with diacetoxyphenylpropene-maleic anhydride **alternating** copolymer, hydrolyzed 67247-04-5DP, reaction products with diacetoxyphenylpropene-maleic anhydride **alternating** copolymer, hydrolyzed 141596-23-8DP, reaction products with amines, hydrolyzed
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and affinity for cell **membranes** of)

IT 13620-82-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and **polymn.** of, with maleic anhydride)

L13 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:602736 HCAPLUS
DOCUMENT NUMBER: 115:202736
TITLE: Membrane affinity purification apparatus and its use in the purification of macromolecules of therapeutic value
INVENTOR(S): Goffe, Randal A.; Zale, Stephen E.; O'Connor, James L.; Kessler, Stephen B.; Cohen, Charles M.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9005018	A1	19900517	WO 1989-US4847	19891030
W: AU, BB, BG, BR, DK, FI, HU, JP, KR, LK, MC, MG, MW, NO, RO, SD, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2001720	AA	19900430	CA 1989-2001720	19891027
AU 8945247	A1	19900528	AU 1989-45247	19891030
EP 483143	A1	19920506	EP 1989-912702	19891030
EP 483143	B1	19940601		
EP 483143	B2	19970409		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 106272	E	19940615	AT 1989-912702	19891030
US 5310688	A	19940510	US 1993-35549	19930323
US 5683916	A	19971104	US 1995-465479	19950605

PRIORITY APPLN. INFO.:

US 1988-265061	19881031
US 1989-428263	19891026
US 1989-428263	19891026
US 1989-428263	19891026
US 1989-428263	19891026
US 1989-428263	19891026
EP 1989-912702	19891030
WO 1989-US4847	19891030
US 1990-487668	19900302
US 1993-83859	19930628

AB An app. is provided which is useful for the sepn. of .gtoreq.1 preselected ligate(s) in a fluid. Also provided is an easily scaled-up membrane affinity sepn. process which is reliable, highly selective, gives a high yield of product, and has a high volumetric throughput. A substantially isotropic porous membrane is used, to which is assocd. a preselected ligand, which provides an optimum loading capacity and low dead vol. while allowing high filtrate flow rates. Methods for isolation of macromols. of therapeutic value, e.g. factor VIII and fibronectin, are described, and diagrams of the app. are included. Cloning and expression of a bifunctional binding site protein (one domain binding digoxin and the other binding Ig Fc regions) are also described. Thus a polyether sulfone/poly(ethylene oxide) hollow-fiber membrane was sequentially reacted with ethylene glycol diglycidyl ether and hydroxyethyl cellulose, activated with 2-fluoro-1-methylpyridinium p-toluenesulfonate, and the activated fibers reacted with an antibody to factor VIII. The resulting membrane was used to purify a factor VIII conc.; the purifn. factor was 115.

IC B01D063-02; B01D063-04; B01D063-08; C07K003-20
CC 9-3 (Biochemical Methods)
Section cross-reference(s): 63

IT Blood-coagulation factors
Interferons
RL: ANST (Analytical study)
(antibody to, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Liposome
Plasmid and Episome
Surfactants
Agglutinins and Lectins
Antibodies
Antigens
Blood-coagulation factors
Hormones
Receptors
RL: ANST (Analytical study)
(**conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Carboxylic acids, compounds
RL: ANST (Analytical study)
(**conjugates**, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Macromolecular compounds
RL: ANST (Analytical study)
(hollow-fiber affinity **membrane** contg., for biomol. sepn., surface property **alteration** in relation to)

IT Polycarbonates, uses and miscellaneous
Polyesters, uses and miscellaneous
Polyimides, uses and miscellaneous
Polyoxyarylenes
Polysulfones, uses and miscellaneous

Urethane **polymers**, uses and miscellaneous
RL: SPN (Synthetic preparation); PREP (Preparation)
(hollow-fiber membranes of, for affinity membrane prepn. for sepn. of biomols.)

IT **Polymers**, uses and miscellaneous
RL: SPN (Synthetic preparation); PREP (Preparation)
(hollow-fibers membrane of, for affinity membrane prepn. for sepn. of biomols.)

IT Bacteria
Plant cell
(surface receptor of, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Immunoglobulins
RL: ANST (Analytical study)
(A, **conjugates**, antibody to, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Proteins, specific or class
RL: ANST (Analytical study)
(A, **conjugates**, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Antigens
RL: ANST (Analytical study)
(CEA (carcinoembryonic antigen), antibody to, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Immunoglobulins
RL: ANST (Analytical study)
(E, **conjugates**, antibody to, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Immunoglobulins
RL: ANST (Analytical study)
(G, **conjugates**, antibody to, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Immunoglobulins
RL: ANST (Analytical study)
(M, **conjugates**, antibody to, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Polymerization
(Ziegler-Natta, **hydrophobic polymer** for hollow-fiber affinity membrane prepn. by)

IT Siloxanes and Silicones, compounds
RL: ANST (Analytical study)
(arom., **conjugates**, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Ligands
RL: ANST (Analytical study)
(**conjugated**, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Avidins
Enzymes
Histones
Immunoglobulins
Monosaccharides
Nucleic acids
Polysaccharides, compounds
Siloxanes and Silicones, compounds
RL: ANST (Analytical study)
(**conjugates**, suROLES **ASSIGcalHistonesROLES** ASS **Nucleic acidsousROL** *Polysaccharides,)

IT Carbohydrates and Sugars, compounds
Glycoproteins, specific or class

Proteins, specific or class
RL: ANST (Analytical study)
(**conjugates**, mbrane **polymers**, for biomol. **sepn.**Glycoproteins, speci)

IT Lymphokines and Cytokines
RL: ANST (Analytical study)
(interleukins, antibody to, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Polymerization
(ionic, **hydrophobic polymer** for hollow-fiber affinity membrane prepn. by)

IT Proteins, specific or class
RL: ANST (Analytical study)
(ligand-binding, **conjugates**, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Antibodies
RL: ANST (Analytical study)
(monoclonal, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Nucleotides, **polymers**
RL: ANST (Analytical study)
(oligo-, **conjugates**, with hollow-fiber membrane **polymers**, for biomol. sepn.)

IT Nucleotides, **polymers**
RL: ANST (Analytical study)
(poly-, **conjugates**, with hollow-fiber membrane **polymers**, for biomol. sepn.)

IT Vinyl compounds, **polymers**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**polymers**, halogenated, hollow-fiber membranes of, for affinity membrane prepn. for sepn. of biomols.)

IT **Polymers**, compounds
RL: ANST (Analytical study)
(polysulfonates, **conjugates**, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Polymerization
(radical, **hydrophobic polymer** for hollow-fiber affinity membrane prepn. by)

IT Polymerization
(ring-opening, **hydrophobic polymer** for hollow-fiber affinity membrane prepn. by)

IT Polymerization
(stepwise, **hydrophobic polymer** for hollow-fiber affinity membrane prepn. by)

IT Dyes
(synthetic, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Animal growth regulators
RL: ANST (Analytical study)
(transforming growth factors, antibody to, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT Fetoproteins
RL: ANST (Analytical study)
(.alpha.-, **conjugates**, antibody to, with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT 9002-61-3, Chorionic gonadotropin 9002-71-5, Thyrotropic hormone
RL: ANST (Analytical study)
(antibody to, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

IT 9004-62-0D, Hydroxyethyl cellulose, linked polysulfone **conjugates**

RL: ANST (Analytical study)
(for affinity hollow-fiber membrane prepn. for biomol. sepn.)
IT 58-85-5D, Biotin, **polymer**-linked **conjugates**
9000-11-7D, Carboxymethyl cellulose, **polymer**-linked **conjugates** 9002-89-5D, Poly(vinyl alcohol), **polymer**-linked **conjugates** 9002-98-6D, **polymer**-linked **conjugates** 9004-34-6D, Cellulose, alkyl ethers, linked-**polymer conjugates** 9004-54-0D, Dextran, **polymer**-linked **conjugates** 9005-49-6D, Heparin, **polymer**-linked **conjugates** 9015-73-0D, Diethylaminoethyldextran, **polymer**-linked **conjugates** 27357-96-6D, **polymer**-linked **conjugates**
RL: ANST (Analytical study)
(in affinity hollow-fiber membrane, for biomol. sepn.)
IT 56-81-5, 1,2,3-Propanetriol, uses and miscellaneous 872-50-4, NMP, uses and miscellaneous
RL: USES (Uses)
(polyether sulfone/poly(ethylene oxide) **polymer** dope contg., for affinity hollow-fiber membrane for biomol. sepn.)
IT 105913-11-9, Plasminogen activator
RL: ANST (Analytical study)
(tissue, antibody to, **conjugates** with hollow-fiber membrane **polymer**, for biomol. sepn.)

L13 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:445683 HCAPLUS
DOCUMENT NUMBER: 115:45683
TITLE: Process and pulsed alternating voltage enzyme electrode sensor for measuring the glucose content of glucose-containing fluids under anaerobic conditions
INVENTOR(S): Kuypers, Martinus Henricus; Steeghs, Gerardus Fransiscus Jozef
PATENT ASSIGNEE(S): PPG Hellige B. V., Neth.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 396788	A1	19901114	EP 1989-108264	19890508

R: AT, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE

AB Glucose is measured in liq. media, esp. blood under anaerobic conditions, using an electrochem. sensor operated with a pulsed alternating voltage switchable between a higher operating voltage level (A), at which excess O is released at the working electrode and into the surrounding immobilized glucose oxidase by way of electrochem. splitting H2O, and a lower operating voltage (B), at which only the catalytic glucose reaction in glucose oxidase takes place to form H2O2 which oxidizes at the working electrode. The current flowing thereby is detd. as the value sensed in the phase of low operating voltage level B and is evaluated as a measure of glucose concn. Other embodiments and diagrams of the sensors are given.
IC ICM C12M001-40
CC 9-7 (Biochemical Methods)
IT **Polymers**, uses and miscellaneous
RL: USES (Uses)
(glucose oxidase immobilized in, in oxygen-producing pulsed alternating

voltage enzyme electrode sensor for glucose detn.)

IT Electrodes
(bio-, enzyme, **membrane**, **hydrophobic**, in oxygen-producing pulsed **alternating** voltage enzyme electrode sensor for glucose detn.)

L13 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:84576 HCAPLUS
DOCUMENT NUMBER: 94:84576
TITLE: Ring-opening polymerization of bicyclic oxalactone and oxalactam. Speciality **polymers** having **hydrophilic**- and **hydrophobic** microdomains
AUTHOR(S): Sumitomo, Hiroshi
CORPORATE SOURCE: Fac. Agric., Nagoya Univ., Nagoya, 464, Japan
SOURCE: Polym. Prepr., Am. Chem. Soc., Div. Polym. Chem. (1979), 20(1), 134-7
CODEN: ACPPAY; ISSN: 0032-3934
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A discussion of the prepn. and properties of macrocyclic oligoesters (dimers, tetramers, and hexamers) obtained by the ring-opening polymn. of 6,8-dioxabicyclo[3.2.1]octan-7-one (I) or optically active (+)-(1R,5R)-I and of a hydrophilic polyamide membrane obtained from 8-oxa-6-azabicyclo[3.2.1]octan-7-one (II) by simultaneous ring-opening polymn. and casting.

CC 35-3 (Synthetic High Polymers)

ST polydioxabicyclooctanone oligoester; polyoxaazabicyclooctanone membrane; polyamide oxaazabicyclooctanone membrane; polyester dioxabicyclooctanone oligomer; cyclic oligomer dioxabicyclooctanone; lactam oxaazabicyclooctanone **polymer**

IT **Membranes** and Diaphragms
(polyamides, contg. **alternating** amide and tetrahydropyran groups, **hydrophilic**)

IT Polyamides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, contg. **alternating** amide and tetrahydropyran groups, as **hydrophilic membranes**)

IT 49793-24-0P 76623-37-5P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and properties of, as **hydrophilic** membrane)

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               DEL HIS Y
L1        109020 S MEMBRANE#
L2          5262 S L1 (6A) (ALTER? OR DISRUPT? OR ENHANC? OR STRUCT?)
L3        443676 S POLYMER##
L4          5262 S L1 AND L2
L5        236933 S TRANSPORT?
L6           226 S L4 AND L5
L7          1452 S L1 (4A) (ALTER? OR DISRUPT? OR ENHANC? (3A) TRANSPOR?)
L8           161 S L7 AND L3
L9             5 S L8 AND ENHANC? (4A) TRANSPOR?
L10            6 S L8 AND CONJUGAT?
L11        33823 S HYDROPHOB?
L12        43851 S HYDROPHIL?
L13           13 S L8 AND L11 AND L12
L14           20 S L13 OR L10 OR L9

     FILE 'WPIDS' ENTERED AT 10:07:39 ON 07 MAR 2002

=> d .wp tech 1-20

L14  ANSWER 1 OF 20  WPIDS COPYRIGHT 2002   DERWENT INFORMATION LTD
AN   2001-602251 [68]    WPIDS
DNC  C2001-178322
TI   Non-naturally occurring gene therapy vector useful for gene therapy,
     comprises an inner shell having a core complex containing a nucleic acid
     and at least one complex forming reagent.
DC   A96 B04 B05 D16
IN   CHENG, C; FREI, J; METT, H; PUTHUPPARAMPIL, S; STANEK, J; SUBRAMANIAN, K;
     TITMAS, R; WOODLE, M; YANG, J
PA   (NOVS) NOVARTIS AG; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH
CYC  94
PI   WO 2001049324 A2 20010712 (200168)* EN  178p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
            DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
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LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001033669 A 20010716 (200169)
ADT WO 2001049324 A2 WO 2000-EP13300 20001228; AU 2001033669 A AU 2001-33669 20001228
FDT AU 2001033669 A Based on WO 200149324
PRAI US 1999-475305 19991230
AB WO 200149324 A UPAB: 20011121
NOVELTY - A non-naturally occurring gene therapy vector, comprising an inner shell having a core complex (1) containing a nucleic acid and at least one complex forming reagent (2), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) forming a self assembling core complex by feeding a stream of a solution of a nucleic acid and a core complex-forming moiety into a static mixer, the streams are split into inner and outer helical streams that intersect at several different points causing turbulence and promoting mixing, that results in a physicochemical assembly interaction; and
(2) a compound having formula (I).
m = 3 or 4;
Y = -(CH2)n-, or -CH2-CH=CH-CH2- if R2 is -(CH2)3-NR4R5 and m is 3;
n = 3-16;
R2 = H, or lower alkyl, or -(CH2)3-NR4R5 is m is 3;
R3 = H, or alkyl, or -CH2-CH(-X')-OH if R2 is -(CH2)3-NR4R5 and m is 3;
X and X' = independently, H or alkyl; and
R, R1, R4 and R5 = independently, H or lower alkyl, where R, R1, R4 and R5 are not all H or methyl, if m is 3 and Y is -(CH2)3.
ACTIVITY - None given.
MECHANISM OF ACTION - Gene therapy.
No biological data is given.
USE - In gene therapy for nucleic acid delivery.
ADVANTAGE - The vectors are stable having an improved outer steric layer that provides enhanced target specificity, in vivo and colloidal stability. The vectors are relatively homogenous and comprises chemically defined species. The vectors demonstrate improved cell entry and intracellular trafficking, permitting enhanced nucleic acid therapeutic activity such as gene expression.
Dwg.0/30
TECH UPTX: 20011121
TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The vector further comprises a fusogenic moiety, an outer shell moiety and a targeting moiety. The vector comprises a mixture of at least two outershell reagents in which each of the outershell reagents comprises the **hydrophilic polymer** having substantially different sizes. The fusogenic moiety is incorporated directly in (1) and comprises a shell that is anchored to (1). The fusogenic moiety comprises at least one moiety selected from a viral peptide, an amphiphilic peptide, a fusogenic **polymer** lipid **conjugate** and a biodegradable fusogenic **polymer**-lipid **conjugate**. The fusogenic moiety is a membrane surfactant **polymer**-lipid **conjugate** selected from Thesit (RTM), Brij 58 (RTM), Brij 78 (RTM), Tween 80 (RTM), Tween 20 (RTM), C12E8, C14E8, C16E8, Chol-PEG 900, analog containing polyoxazoline or other **hydrophilic polymer** substituted for the PEG and analog having fluorocarbons substituted for the hydrocarbon.
CnEn = hydrocarbon poly(ethylene glycol) ether;
C = hydrocarbon of carbon length N; and
E = poly(ethylene glycol) of degree of polymerization N.
The inner shell is anchored to the outer shell moiety via a covalent linkage that is degradable by chemical reduction or sulfhydryl treatment

at a pH of at most 6.5. The covalent linkage is selected from -C(O)-NH-N=CH-, -C(O)-NH-NH-C(O)-NH=CH-, -O-T-CH=N-NH-C(O)- or -NH-C(O)-CH2-CH2-S-S-. The outer shell moiety stabilizes the vector and reduces nonspecific binding to proteins and cells. The outer shell moiety is anchored to the fusogenic moiety and (1) and comprises a **hydrophilic polymer**. The outer shell comprises the targeting moiety. The outer shell comprises a protective **polymer conjugate** in which the **polymer** exhibits solubility in both polar and non-polar solvents. The targeting moiety enhances binding of the vector to a target tissue and cell population. The targeting element is a receptor ligand, an antibody or antibody fragment, a targeting peptide, a targeting carbohydrate molecule or a lectin, preferably vascular endothelial cell growth factor, fibroblast growth factor (FGF)2, somatostatin and its analog, transferrin, melanotropin, ApoE and ApoE peptide, von Willebrand's Factor and von Willebrand's Factor peptide; adenoviral fiber protein and adenoviral fiber protein peptide; PD1 and PD1 peptide, epidermal growth factor (EGF) and EGF peptide, RGD peptide, folate, pyridoxyl, sialyl-Lewis and chemical analogs. (2) is selected from a lipid, a **polymer**, and a spermine analog complex of (I). The complex-forming lipid agent is selected from phosphatidylcholine, phosphatidylethanolamine, dioleoylphosphatidylethanolamine, dioleoylphosphatidylcholine, cholesterol and other sterols, N-1-(2,3-dioleyloxy)propyl-N,N,N-trimethylammonium chloride, 1,2-bis(oleoyloxy)-3-(trimethylammonia) propane, phosphatidic acid, phosphatidylglycerol, phosphatidylinositol, glycolipids comprising two optionally unsaturated 14-22C hydrocarbon chains, sphingomyelin, sphingosine, ceramide, terpenes, cholesterol hemisuccinate, cholesterol sulfate, diacylglycerol, 1,2-dioleoyl-3-dimethylammonium propanediol, dioctadecyldimethylammonium bromide, dioctadecyldimethylammonium chloride, dioctadecylamidoglycylspermine, 1,3-dioleoyloxy-2-(6-carboxyspermyl)propylamide, Lipofectamine7 (RTM) (2,3-dioleyloxy-N-(2-(sperminecarboxamido)ethyl)-N,N-dimethyl-1-propanaminium trifluoroacetate), hexadecyltrimethyl-ammonium bromide, dimethyl-dioctadecylammonium bromide, 1,2-dimyristyloxypropyl-3-dimethyl-hydroxy ethyl ammonium bromide, dipalmitoylphosphatidylethanolamylspermine , dioctylamineglycinespermine, dihexadecylamine-spermine (C18-2-Sper), aminocholesterol-spermine, 1-(2-(9(Z)-octadecenoyloxy)ethyl)-2(8(Z)-heptadecenyl)-3-(2-hydroxyethyl)imidazolinium chloride, dimyristoyl-3-trimethylammonium-propane, 1,2-dimyristoyl-sn-glycero-3-ethylphosphatidylcholine, lysylphosphatidylethanolamine, cholestryl-4-aminoproprionate, Genzyme-67 (spermadine cholestryl carbamate), 2-(dipalmitoyl-1,2-propandiol)-4-methylimidazole, 2-(dioleoyl-1,2-propandiol)-4-methylimidazole, 2-(cholestryl-1-propylamine carbamate)imidazole, N-(4-pyridyl)-dipalmitoyl-1,2-propandiol-3-amine, 3-beta-(N-(N',N'- dimethylaminoethane)carbamoyl)cholesterol, 3beta-(N-(N',N',N'-trimethylaminoethane)carbamoyl) cholesterol, 1,2-dioleoyl-sn-glycero-3-succinate, 1,2-dioleoyl-sn-glycero-3-succinyl-2-hydroxethyl disulfide ornithine **conjugate**, 1,2-dioleoyl-sn-glycero-3-succinyl-2-hydroxethyl hexyl orithine **conjugate**, N,N',N,N'-tetramethyl-N,N',N,N'-tetrapalmityolspermine, 3-tetradecylamino-N-tert-butyl-N'- tetradecylpropionamidine (vectamidine or diC14-amidine), YKS-220 (RTM) (N-(3-(2-(1,3-dioleoyloxy)propoxy-carbonyl)propyl)-N,N,N-trimethyl ammonium iodide) and DC-6-14 (RTM) (O,O'-ditetradecanoyl-N-(alpha-trimethylammonioacetyl)diethanolamine chloride). (2) comprises a mixture of at least two (2). (2) possesses at least one additional activity selected from cell binding, biological **membrane** fusion, endosome **disruption** and nuclear targeting. The nucleic acid is selected from a recombinant plasmid, a replication-deficient plasmid, a mini-plasmid, a recombinant viral genome, a linear nucleic acid fragment, an antisense agent, a linear

polynucleotide, a circular polynucleotide, a ribozyme, a cellular promoter and a viral genome. (2) further comprises a nuclear targeting moiety that enhances nuclear binding and/or uptake. The nuclear targeting moiety is selected from a nuclear localization signal peptide, a nuclear membrane transport peptide or a steroid receptor binding moiety. The nuclear targeting moiety is anchored to the nucleic acid in (1). The viral peptide is selected from MLV env peptide, HA env peptide, a viral envelope protein ectodomain, a membrane-destabilizing peptide of a viral envelope protein membrane-proximal domain, a **hydrophobic** domain peptide segment of a viral fusion protein or an amphiphilic-region containing peptide. The amphiphilic-region containing peptide is selected from melittin, magainins, fusion segments from Haemophillus influenza hemagglutinin (HA) protein, human immunodeficiency virus (HIV) segment I from the cytoplasmic tail of HIV 1gp41 or amphiphilic segments from viral env membrane proteins.

TECHNOLOGY FOCUS - **POLYMERS** - Preferred Components: The fusogenic moiety comprises a fusogenic **polymer**, a fusogenic **polymer** lipid-**conjugate**, a biodegradable fusogenic **polymer** or a biodegradable fusogenic **polymer**-lipid **conjugate**. (2) is a **polymer** of structure -(-N(R1)-CH2-R2-)x-(-N(R3)-CH2-R2-)y-. The fusogenic moiety is a **polymer** of structure -(-N(R1)-CH2-R2-)x-(-N(R'3)-CH2-R2-)y-.

R1 and R3 = hydrocarbon optionally substituted with amine, guanidinium or imidazole moiety;

R2 = lower alkyl;

x and y = not defined;

R'3 = hydrocarbon optionally substituted with carboxyl, hydroxyl, sulfate or phosphate.

The outer shell comprises a protective steric **polymer** **conjugate** in which the **polymer** is selected from the group consisting of polyethylene-glycol (PEG), a polyacetal **polymer**, a polyoxazoline **polymer** optionally block with end-group **conjugation**, a hydrolyzed dextran polyacetal **polymer**, a polyoxazoline, a polyethylene glycol, a polyvinylpyrrolidone, polylactic acid, polyglycolic acid, polymethacrylamide, polyethyloxazoline, polymethyloxazoline, polydimethylacrylamide, polyvinylinethylether, polyhydroxypropyl methacrylate, polyhydroxypropylmethacrylamide, polyhydroxyethyl acrylate, polyhydroxyethyloxazoline, polyhydroxypropyloxazoline, polyaspartamide or a polyvinyl alcohol.

L14 ANSWER 2 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-596316 [67] WPIDS
DNC C2001-176449
TI Composition, for **disruption** of cell **membrane**, used for delivering diagnostic or therapeutic agents to cytoplasm of cells, contains **hydrophobic** **polymer** and **hydrophilic** component coupled via linkage which is cleaved as function of pH.
DC A96 B07
IN HOFFMAN, A S; MURTHY, N; STAYTON, P S
PA (UNIW) UNIV WASHINGTON
CYC 93
PI WO 2001051092 A2 20010719 (200167)* EN 50p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001027648 A 20010724 (200168)

ADT WO 2001051092 A2 WO 2001-US356 20010105; AU 2001027648 A AU 2001-27648 20010105
FDT AU 2001027648 A Based on WO 200151092
PRAI US 2000-174893P 20000107
AB WO 200151092 A UPAB: 20011119
NOVELTY - Composition, for **disruption** of **membrane**, contains **conjugate** comprising:
(1) **Polymer** which is **hydrophobic** under conditions where **membrane** is to be **disrupted**; and
(2) **Hydrophilic** component which is an agent to be delivered, or groups/**polymer** linkable/linked to **hydrophobic polymer**, in amount making **conjugate hydrophilic**.
The **hydrophilic** component is coupled to **hydrophobic polymer** via linkage which is cleaved as function of pH.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for a method of producing the composition and a method of disrupting a cell or organelle using the composition.
USE - The composition is used for delivering diagnostic or therapeutic agents, through cell membranes; barriers; or layers, to cytoplasm of cells, and for the release of cell contents for subsequent recovery and/or analysis.
ADVANTAGE - The composition can deliver agents to cells without significant lysosomal degradation, and can be controlled externally by non-invasive means such as ultrasound.
Dwg.0/6
TECH UPTX: 20011119
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The **hydrophilic** component is a therapeutic, diagnostic, or prophylactic agent to be delivered to a cell or organelle, preferably a protein, peptide, nucleotide, saccharide, polysaccharide, preferably a nucleotide molecule selected from antisense, ribozyme, ribozyme guide sequence, triplex forming nucleotide and gene, complexed to a **polymer** component of the **conjugate**. The **hydrophobic polymer** is vinyl-type, non-vinyl , or naturally derived. The **hydrophilic** group is a hydroxy acid, thiol, amine, carboxyl, or amino acid. The **conjugate** further comprises a ligand specifically binding to a target molecule and the composition further comprises a carrier selected from carriers for systemic, local, or topical delivery of the **conjugate**.
Preferred Linkages: The **hydrophilic** groups are coupled directly to the **hydrophobic polymer**. The linkage coupling the **hydrophilic** to the **membrane disruptive** component is dissruptable upon exposure to physical or chemical stimulus, it is preferably stable at pH 6.8 - 8, disrupted at pH less than 6.5, hydrolyzes within 30 - 60 minutes at pH 5.0 - 5.5, and is acetal, orthoester, cis-aconityl, carboxylic acid hydrazone, phosphamide, ester, Schiff base, vinyl ether, dithioacetal, tert butyl ester, carbamate, urethane, anhydride, polysaccharide, amide, ester, ether, thiourea, urea, thioester, sulfenamide, phosphoroamidate, or amine N-oxide. The agent to be delivered is coupled to the **hydrophilic** or **membrane disruptive** component by a degradable or dissruptable linkage, preferably degradable by change in pH.
Preferred Cell: The cell is in a patient, an endosome in a cell, or a bacterial cell.

L14 ANSWER 3 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-582012 [65] WPIDS
DNC C2001-172537
TI Compositions and methods for enhancing drug delivery across biological

membranes, using a delivery-**enhancing** **transporter** having guanidino or amidino moieties.

DC B05

IN ROTHBARD, J B; WENDER, P A

PA (CELL-N) CELLGATE INC; (ROTH-I) ROTHBARD J B; (WEND-I) WENDER P A

CYC 94

PI WO 2001062297 A1 20010830 (200165)* EN 54p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001036920 A 20010903 (200202)
US 2002009491 A1 20020124 (200210)

ADT WO 2001062297 A1 WO 2001-US4459 20010209; AU 2001036920 A AU 2001-36920 20010209; US 2002009491 A1 Provisional US 2000-182166P 20000214, US 2001-779693 20010207

FDT AU 2001036920 A Based on WO 200162297

PRAI US 2001-779693 20010207; US 2000-182166P 20000214

AB WO 200162297 A UPAB: 20011108

NOVELTY - Drug delivery across biological membranes and tissues, particularly across 1 or more layers of skin, is **enhanced** using delivery-**enhancing** **transporters** having guanidino or amidino moieties.

DETAILED DESCRIPTION - A method for delivery of a compound to the surface of, into or across a biological barrier, comprises contacting the barrier with a composition comprising the compound and a delivery **enhancing** **transporter** comprising sufficient guanidino or amidino moieties to increase delivery of the compound compared to delivery in the absence of the transporter. An INDEPENDENT CLAIM is included for a composition comprising a biologically active agent and a delivery **enhancing** **transporter** comprising guanidino or amidino moieties.

ACTIVITY - Antiinflammatory; antiulcer; antiallergic; antiasthmatic; vasotropic; antiparkinsonian; neuroleptic; cytostatic; anti-HIV; anticonvulsant; neuroprotective; tranquilizer; vulnerary; antidepressant; nootropic; antimigraine; analgesic.

MECHANISM OF ACTION - H2 histamine inhibitor; proton-potassium ATPase inhibitor.

The ability of polyArg to facilitate cellular uptake of small organic acids was determined. In separate vials, n equivalents (n = 1-6) of fluorescein (poorly soluble in water) were added to the free base of a nonamer of arginine in water. Phosphoric acid (6-n equivalents) was added to each flask and the solutions were frozen and lyophilized. When the dried powders were taken up in water, they were very water soluble. The 8 compounds had fluorescein:peptide ratio from 1:1 to 6:1.

When dilutions of each of the solutions were used in cellular uptake assays, the resultant cells were stained equivalently, showing that all fluorescein molecules were deposited on the cell surface. The staining pattern of the cells was different when compared to fluorescein that was covalently attached to short **polymers** of arginine. Distinct punctate staining was seen on the cell surface as well as in the cytosol, when covalent **conjugates** were used. Staining of individual cells was very heterogeneous, with the variation in cell fluorescence ranging over 3 orders of magnitude. However, when noncovalent **conjugates** were used, cell staining was uniform with cell fluorescence varying only by a factor of 2-4. Staining was intense, with the majority of the dye on the cell surface.

USE - For delivery of drugs and diagnostic imaging or contrast

agents, across biological membranes and tissues, e.g. cell membranes, mitochondrial membranes, dermal and epithelial membranes, and across the blood-brain barrier. The compound may be delivered into and across the stratum corneum, stratum ganulosum, stratum lucidum and/or stratum germinativum.

The compositions can be used to treat e.g. Crohn's disease, ulcerative colitis, gastrointestinal ulcers, peptic ulcer disease or abnormal proliferative disease; a bronchial condition (e.g. cystic fibrosis, asthma, allergic rhinitis and chronic obstructive pulmonary disease); ischemia, Parkinson's disease, schizophrenia, cancer, acquired immune deficiency syndrome, infections of the central nervous system, epilepsy, multiple sclerosis, neurodegenerative disease, trauma, depression, Alzheimer's disease, migraine, pain or a seizure disorder. Dwg.0/5

TECH UPTX: 20011108

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Drugs: The drug is an antiviral agent, e.g. acyclovir, famciclovir, ganciclovir, foscarnet, idoxuridine, sorivudine, trifluridine, valacyclovir, cidofovir, didanosine, stavudine, zalcitabine, zidovudine, ribavirin or rimantatine; an antibacterial agent, e.g. nafcillin, oxacillin, penicillin, amoxicillin, ampicillin, cefotaxime, ceftriaxone, rifampin, minocycline, ciprofloxacin, norfloxacin, erythromycin or vancomycin; an antifungal agent, e.g. amphotericin, itraconazole, ketoconazole, miconazole, nystatin, clotrimazole, fluconazole, ciclopirox, econazole, naftifine, terbinafine or griseofulvin; an antineoplastic agent, e.g. pentostatin, 6-mercaptopurine, 6-thioguanine, methotrexate, bleomycins, etoposide, teniposide, dactinomycin, daunorubicin, doxorubicin, mitoxantrone, hydroxyurea, 5-fluorouracil, cytarabine, fludarabine, mitomycin, cisplatin, procarbazine, dacarbazine, paclitaxel, colchicine or vinka alkaloids; immunosuppressive agents, e.g. methotrexate, azathioprine, fluorouracil, hydroxyurea, 6-thioguanine, cyclophosphamide, mechloroethamine hydrochloride, carmustine, cyclosporine, taxol, tacrolimus, vinblastine, dapsone or sulfasalazine; an analgesic agent, e.g. lidocaine, bupivacaine, novocaine, procaine, tetracaine, benzocaine, cocaine, mepivacaine, etidocaine, proparacaine, ropivacaine or prilocaine; a vitamin; or hormone. Preferred **Transporter**: The delivery **enhancing transporter** is preferably a peptide having 6-15 amino acid residues, where 6-12 are selected from L-arginine, D-arginine, L-homoarginine or D homoarginine.

Preferred Method: The compound is an H2 histamine inhibitor, an inhibitor of the proton-potassium ATPase or an antibiotic directed at Helicobacter pylori. The compound is delivered into and across stratum corneum, stratum granulosum, stratum lucidum or stratum germinativum. The compound is a diagnostic or contrast agent.

L14 ANSWER 4 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-091577 [10] WPIDS
DNC C2001-027033
TI Electrochemical sensor for subcutaneous implantation into a mammal's body to measure an analyte in subcutaneous fluid has working electrode and analyte responsive sensing layer contacting with the analyte only at an edge of the sensor.
DC B04 D16
IN AUDETT, J D; CHO, B; SAKSLUND, H; SAY, J; TOMASCO, M F; YAMASAKI, D
PA (THER-N) THERASENSE INC
CYC 92
PI WO 2000078992 A2 20001228 (200110)* EN 42p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ

EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000057471 A 20010109 (200122)
ADT WO 2000078992 A2 WO 2000-US16773 20000616; AU 2000057471 A AU 2000-57471 20000616
FDT AU 2000057471 A Based on WO 200078992
PRAI US 2000-194618P 20000405; US 1999-139936P 19990618
AB WO 200078992 A UPAB: 20010220
NOVELTY - An electrochemical sensor (100), comprising a working electrode (104) and an analyte-responsive sensing layer (134) near the working electrode, is new. The sensing layer is exposed to contact with the analyte only at an edge of the sensor. The sensor signal is limited, at least in part, by mass transport of an analyte to the sensing layer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of determining the concentration of an analyte in a body fluid of a mammal, comprising:

(a) implanting at least a portion of the novel electrochemical sensor into the body of a mammal so that the edge of the sensor contacts body fluid of the mammal; and

(b) measuring the concentration of the analyte in the body fluid using the sensor.

USE - For subcutaneous implantation into the body of a mammal for contact with body fluids of the mammal to measure an analyte in subcutaneous fluid (claimed).

ADVANTAGE - The invention restricts the mass transport of the analyte to the sensing layer eliminating the need for a mass **transport** limiting **membrane**. The **enhancement** of operational stability and operational life of the sensor includes:

(a) reduced flux of analyte to the sensing layer which reduces the rate of enzyme turnover;

(b) deeper diffusion of glucose into the sensing layer to reach relatively unused enzyme as enzyme at the edge of the sensing layer is deactivated during use;

(c) the immobilization of the sensing layer between the base and top layers which limits the swelling of a hydrogel; and

(d) the reduction of the risk of the enzyme leaching into tissue.

DESCRIPTION OF DRAWING(S) - The figure shows a perspective view of an analyte sensor.

Electrochemical sensor 100
Sensor body 101
Working electrode 104
Reference/counter electrode 108
Top surface 111
Base layer 112
Base layer 113
Top layer 116
Proximal end 120
Distal edge 124
Side edge 128
Analyte-responsive sensing layer 134.

Dwg.1/16
TECH UPTX: 20010220
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Device: The sensor has a flexible body (101) having an inner peripheral surface extending into the sensor. The edge, is a peripheral edge, side edge (128), or preferably a distal edge (124) of the sensor, which is planar or preferably cylindrical. T edge at which the sensing layer is exposed is defined by at least a portion of the inner peripheral surface. The sensor has a base layer (113) and an oxygen permeable top layer (116), both

layers being impervious to analyte, and a less than 100, preferably 1-10 micro-m thick spacer layer. The sensing layer is non-leachably disposed on the sensor. The sensing layer and the spacer layer are at least partially disposed between these base and top layers. The spacer layer defines a channel with a peripheral surface extending into the spacer layer, and the edge at which the sensing layer is exposed is defined by at least a portion of this inner peripheral surface.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Materials: The analyte is glucose, and the sensing layer comprises a redox **polymer**, an enzyme, and a cross-linker.

L14 ANSWER 5 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-031893 [04] WPIDS
DNC C2001-009771
TI **Hydrophilic** charged microporous membrane useful as filter device for removing bacterial contaminants from water, saline solution, comprises porous **hydrophobic** substrate and coating of charge-providing agent.
DC D15 J01
IN ISHEE, M; KINSEY, J L; KONSTANTIN, P; SHERTOK, J; WU, X; YANG, Y
PA (PALL) PALL CORP
CYC 92
PI WO 2000069549 A1 20001123 (200104)* EN 42p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000050036 A 20001205 (200113)
ADT WO 2000069549 A1 WO 2000-US12894 20000512; AU 2000050036 A AU 2000-50036 20000512
FDT AU 2000050036 A Based on WO 200069549
PRAI US 1999-134197P 19990514
AB WO 200069549 A UPAB: 20010118
NOVELTY - A **hydrophilic** charged microporous membrane comprises a porous **hydrophobic** substrate and a coating comprising charge-providing agent.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (i) preparing **hydrophilic** charged microporous membrane by contacting porous **hydrophobic** substrate with composition containing charge-providing agent or its precursor; (ii) device comprising **hydrophilic** charged membrane; and (iii) process for treating fluid containing bacterial contaminants by placing fluid in contact with the **hydrophilic** charged microporous membrane and recovering a bacterial contaminant depleted fluid.
USE - As filter device (claimed) for separation, or removal of bacterial contaminants from water, saline solution and other fluids. For filtering biological fluid such as lymph and cerebrospinal fluid and pharmaceutical products such as composition containing proteins (e.g. antibodies, enzyme, vaccines), amino acids, peptides, nucleic acids, plasmids, cosmids, phages, polysaccharides, lipids, bioreactor, fermenter and/or cell culture harvests.
ADVANTAGE - The membrane has effective endotoxin retaining capacity, water and/or saline solution wettability and water permeability.
Dwg.0/7
TECH UPTX: 20010118
TECHNOLOGY FOCUS - **POLYMERS** - Preferred Component: The **hydrophobic** substrate or matrix is a **polymer** such as

polyethersulfone substrate or matrix. The charge-providing agent is distributed within **hydrophobic polymer** matrix. The porous **hydrophobic** substrate (substantially) free of wetting agent. Preferred Agent: The charge-providing agent is positively charged or negatively charged. The positively charged agent is positively charged **polymer** (PCP). The PCP contains quarternary ammonium groups. The PCP is polyamine (or acrylic **polymer**) containing quarternary ammonium groups. The polyamine is crosslinked through ring opened epoxy groups. The acrylic **polymer** comprising polymerized acrylol monomer preferably alkacryloyl monomer, more preferably alkacryloylaminoalkyl monomer is crosslinked through a polyfunctional crosslinking agent (such as alkylene glycol diacrylate). A negatively charged **polymers** comprises sulfonic acid groups, preferably polymerized acrylamido sulfonic acid monomer. The negatively charged **polymer** is cross linked by acrylamidione cross linking agent (such as N-(alkoxymethyl) acrylamide. The negatively charged **polymer** further includes polymerized hydroxyalkylarcylate monomer or polyacrylate such as ethylene glycol or dimethyl acrylate . Preferred **Polymer** : The **polymer** is poly aromatics, polysulfones, polyolefins, polystyrenes, polyamides, polyimides, fluoropolymers, polycarbonate, polyesters or cellulose acetate. Preferred Process: In the coating process the substrate is contacted with composition containing charge-providing agent and cured and the membrane is extracted to remove the residue. **Alternately** the **hydrophilic** charged microporous **membrane** is obtained by forming a casting solution containing **polymer** capable of forming porous **hydrophobic** matrix, solvent for **polymer**, pore former, and charge-providing agent or its precursor. The casting solution is shaped to obtain a pre-membrane by causing phase-inversion to obtain a phase-inverted membrane. The phase-inverted membrane is leached. Preferred Precursor: The precursor comprises a free radical polymerizable monomer, a crosslinking agent and free radical initiator. The free radical polymerizable monomer is positively charged acrylic monomer containing quarternary ammonium group or negatively charged free radical polymerizable monomer containing sulfonic acid group. The cross linking agent is polyacrylate preferably diacrylate such as alkylene glycol diacrylate.

TECHNOLOGY FOCUS - ENVIRONMENT - Preferred Contaminated Fluid: The fluid contaminated with bacteria is water or pharmaceutical product such as saline solution with surface tension of 72-78 dynes/cm.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Contaminants: The bacterial contaminant comprises an endotoxin.

L14 ANSWER 6 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-389642 [34] WPIDS
CR 2000-423196 [36]
DNC C2000-118513
TI Compositions comprising membrane- and micelle forming lipids for delivering pharmaceuticals to organisms.
DC A96 B02 B07
IN LEIGH, S
PA (PHAR-N) PHARES PHARM RES NV
CYC 1
PI GB 2344520 A 20000614 (200034)* 13p
ADT GB 2344520 A GB 1998-27006 19981208
PRAI GB 1998-27006 19981208
AB GB 2344520 A UPAB: 20000801
NOVELTY - A composition (I) for delivering a biologically active compound to an organism, comprising a pharmaceutically active compound dissolved or

dispersed in a lipid and a **polymer** for modifying the swelling properties of the composition and/or for rendering the composition comminutable or friable, is new.

ACTIVITY - Variable

MECHANISM OF ACTION - Pharmaceutical carrier.

No data given.

USE - The composition (I) is used for delivering pharmaceutically active agents, such as nifedipine and griesofulvin (claimed), to a patient.

ADVANTAGE - (I) has improved physiological properties and loading capacities allowing the development of novel dosage forms. (I) provides maximum bioavailability with minimum side effects. It is an improved carrier for both lipophilic and **hydrophobic** active compounds that is safe, effective and may provide benefits in a range of applications.

In particular, (I) provides:

(1) enhanced ability to effect molecular solution of poorly water soluble compounds;

(2) enhanced absorption of both **hydrophilic** and lipophilic compounds through lipid-**membrane** interactions and **altered** permeability; and

(3) longer in vivo retention of the hydrated lipid associate on absorption surfaces.

Dwg.0/0

TECH UPTX: 20000718

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (I) may be in comminuted form, spheroidized form, pellet form or in the form of a tablet or capsule.

(I) preferably comprises at least 1 therapeutically active compound and at least 1 micelle-forming lipid. The compound is at least partly in suspension on the lipid (preferably a mixture of membrane lipids and micelle-forming lipids).

The therapeutically active compound is nifedipine or griesofulvin depending on the mix of membrane lipids and micelle-forming lipids utilized.

TECHNOLOGY FOCUS - **POLYMERS** - Preferred Composition: The **polymer** comprises 1-50% by weight (wt%) of the composition. The **polymer** is a methacrylic resin, a povidine, a cellulose derivative, a polyvinyl alcohol and/or polyvinyl phthalate or is a gum. preferably, it is an acrylic **polymer** whose degree of swelling depends on the pH.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Composition: The lipid is a membrane lipid and/or a micelle forming lipid. They are monoacyl lipids and diacyl lipids present in the weight ratio of 1:99 to 99:1 (preferably 1:10 to 10:1).

The lipid comprises 1-20 wt% (especially 10 wt%) of the composition.

Preparation:The monoacyl and diacyl lipids are a mixture obtained by enzyme hydrolysis.

L14 ANSWER 7 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2000-389588 [34] WPIDS

DNN N2000-291751 DNC C2000-118496

TI Specific immunoblotting test for protein antigens, used particularly to detect erythropoietin in sportsmen, with transfer of bound primary antibody to second membrane before detection.

DC A96 B04 D16 J04 S03

IN LASNE, F

PA (HOSP-N) HOSPICES CIVILS LYON ETAB

CYC 1
PI FR 2786273 A1 20000526 (200034)* 31p
ADT FR 2786273 A1 FR 1998-14864 19981120
PRAI FR 1998-14864 19981120
AB FR 2786273 A UPAB: 20000718
NOVELTY - A qualitative and/or quantitative immunoblotting assay of one or more target protein antigens (Ag) in which complexes formed on a first membrane are dissociated and the released primary antibodies (Ab1) are transferred to a transfer membrane (Mt) where they are detected by reaction with secondary antibody (Ab2) is new.

DETAILED DESCRIPTION - A qualitative and/or quantitative immunoblotting assay of one or more target protein antigens (Ag) in which complexes formed on a first membrane are dissociated and the released primary antibodies (Ab1) are transferred to a transfer membrane (Mt) where they are detected by reaction with secondary antibody (Ab2) is new. The test sample is applied to a membrane (Mdb) directly or Ag are separated (from each other and form other proteins) on at least one separation support (Ss) and transferred to an absorption membrane (Mwb) to form an image of Ss. Mdb or Mwb is saturated, preferably with a solution of inert protein, then reacted with one or more specific Ab1 to form complexes. The membranes are then washed to remove unbound Ab1. The bonds in any Ag/Ab1 complexes on the **membrane** are then broken by **altering** the physico-chemical conditions and/or the environment in and on the membrane and released Ab1 are transferred, particularly by desorption, to Mt, leaving Ag and other proteins on the first membrane, therefore forming an image of Ab1 on Mt. The transferred Ab1 are then reacted with Ab2, Mt washed to remove unbound Ab2 and any formation of Ab1/Ab2 complexes detected. Optionally the information is captured on at least one other support, particularly by exposure of a sensitive film.

INDEPENDENT CLAIMS are also included for the following:
(1) device for transfer of released Ab1 to Mt; and
(2) kit for performing the assay including the device of (a).

USE - The method is particularly used to detect (recombinant) erythropoietin or other illicit drugs in humans or animals, especially to detect drug abuse by sportsmen, but may also be used to detect cellular, serum or viral proteins.

ADVANTAGE - Transfer of Ab1 to a separate membrane overcomes the problem of false positives associated with non-specific reaction of Ab2 with other proteins on the membrane, since an Ag/Ab1/Ab2 complex is never formed on the first membrane. The method is generally applicable (to any antigen of Ab2), provides high detection sensitivity for targeted Ag and is simple and economical to perform.

Dwg.0/5

TECH UPTX: 20000718
TECHNOLOGY FOCUS - BIOLOGY - Preferred conditions: The initial complex is disrupted by reducing the pH to 4 or lower, particularly 1-5 (sic) for a temperature of 15-25 degreesC. The disruption (and subsequent) steps are performed as soon as primary complexes are detected on the first membrane. Preferably before transfer of released Ab1, the first membrane and Mt are placed face-to-face, under pressure, and Mt is saturated before treatment with Ab2.

Preferred Materials: All membranes are of natural or synthetic **polymers**. Ab2 are labeled with a chemiluminescent system, e.g. with biotin for subsequent reaction with streptavidin/peroxidase **conjugate** and then chemiluminescent substrate. Ag are particularly (recombinant) erythropoietin (EPO) or cellular, serum or viral proteins, or their mixtures. Agents for saturating membranes are e.g. skim milk or serum albumin, and suitable test samples, optionally diluted, are blood, urine, saliva, cerebro-spinal fluid, cell culture media and intracellular fluids.

Preferred Process: Where Ag are separated initially, this is by electrophoresis or isoelectric focusing.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Device: The device of (1) consists of two plates that retain, in sandwich fashion, the first and second membranes in face-to-face contact. Preferably it also includes an arrangement for wetting the membranes, particularly a piece of absorbent paper soaked in liquid medium.
TECHNOLOGY FOCUS - **POLYMERS** - Suitable membrane materials are halogenated polyalkylidenes (e.g. poly(vinylidene fluoride)) or optionally modified cellulose (e.g. nitrocellulose and/or cellulose acetate).

L14 ANSWER 8 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-633730 [54] WPIDS
DNC C1999-185055
TI New **conjugate** of lipid with basic, **membrane-disrupting** peptide having reversed amide backbone, used to introduce anionic macromolecules or active agents into cells, e.g. for gene therapy.
DC B04 D16
IN KITAS, E A; SCHLAEGER, E
PA (HOFF) ROCHE DIAGNOSTICS GMBH
CYC 84
PI WO 9951629 A2 19991014 (199954)* EN 23p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9937065 A 19991025 (200011)
EP 1068225 A2 20010117 (200105) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
ADT WO 9951629 A2 WO 1999-EP2361 19990407; AU 9937065 A AU 1999-37065 19990407; EP 1068225 A2 EP 1999-919208 19990407, WO 1999-EP2361 19990407
FDT AU 9937065 A Based on WO 9951629; EP 1068225 A2 Based on WO 9951629
PRAI EP 1998-124837 19981230; EP 1998-106302 19980407
AB WO 9951629 A UPAB: 19991221
NOVELTY - **Conjugates** of (i) lipid and (ii) basic, **membrane-disrupting** peptides, and their salts, are new.
DETAILED DESCRIPTION - **Conjugates** of (i) lipids and (ii) basic, **membrane-disrupting** peptides of formula (I) and their salts, comprise:
R1 and R2 = residues of linear or branched, saturated or unsaturated aliphatic carboxylic acids or phospholipids;
R3 = basic, **membrane-disrupting** peptide with a reversed amide backbone;
Y = 2-10C alkylene;
X = CONH or SS
INDEPENDENT CLAIMS are also included for the following:
(a) the peptide QQRKRKIWSILAPLGTTLVKLVAGIC-NH2 (II) with a reversed amide backbone and with at least 50% of residues D-amino acids, and its derivatives;
(b) compositions containing (I), at least one of helper lipid, short-chain phospholipid and/or cationic lipid, optionally also an additional transfection reagent; and
(c) process for introducing into a cell, in vivo or in vitro, an anionic macromolecule (III) or a biologically active anionic molecule (IIIa), by treating the cells with (III) or (IIIa) in presence of (I).
ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - (I) are used to introduce, into eukaryotic or prokaryotic cells, in vivo or in vitro, anionic macromolecules, particularly nucleic acids, or biologically active anionic molecules. In particular DNA (for gene therapy or recombinant protein production), antisense sequences, haptamers, triplex-formers, ribozymes etc. also proteins and peptides (for immunization) are introduced.

ADVANTAGE - Transfection with (I) provides rapid expression of heterologous proteins in large scale systems, with both adherent and suspended cells, even at low DNA concentrations and without significant inhibition by conditioned medium. A **conjugate** prepared from 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine N-(3-(2-pyridyldithio)propionate and the all D reversed-backbone peptide QQRKRKIWSILAPLGTTLVKLVAGIC-NH2 was formulated with a plasmid encoding the human tumor necrosis receptor protein p55 and used to transfect HEK293(EBNA) cells. At a **conjugate** concentration of 10 mg/ml, cell viability was 90-95% with p55 expression 83 ng/ml.

Dwg.0/0

TECH UPTX: 19991221

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compounds: In (I), R1 and R2 are acyl residues of a 12-20C carboxylic acids, especially lauroyl, palmitoyl, stearoyl or oleoyl; X = disulfide; R3 = R3'-CH(CONH2)-CH2-; R3' = residue of (II) without terminal Cys.

Preferred peptide: (II) has all amino acids, except Gly, in D-configuration.

Preparation: Either;

(i) R3NH2 is reacted with a carboxy-lipid (i.e. (I) with XR3 replaced by carboxy); or

(ii) R3SH is reacted with a derivatized lipid, i.e. (I) with XR3 replaced with -SZ, where Z is a leaving group such as 2-pyridylthio.

The lipid derivatives are known from Biochim. Biophys. Acta, 862 (1986) 435, and the peptides are produced by standard methods of solid-phase synthesis.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compositions: These also include (III), particularly a polynucleotide, and optionally also a polycationic **polymer**, particularly poly(ethylene imine). They are formulated as aqueous or organic solutions or dispersions, or as a liposome or micelle. Helper lipids are e.g. phosphatidyl ethanolamines and short phospholipids are dicapryl- or dicaproyl-phosphatidyl choline. The optimal mole ratio of (I):helper lipid is 1-10; of helper lipid:short phospholipid 2:20 and of (I) and additional transfection component 0.1:10.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: For transfection with nucleic acid, the ratio of positive charges to negative charges between (I) and (III) is 0.1-10, preferably 0.5-5, typically using 0.1-10, especially 0.2-2, mg of (III) per 10^4 cells, in vitro, or doses of 0.0001-1 g in vivo.

L14 ANSWER 9 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-540689 [45] WPIDS
DNN N1999-400749 DNC C1999-157934
TI Ion conductive matrixes for forming membranes, composite electrode, electrochemical cell, fuel cell and water electrolizer.
DC A32 A85 E16 E36 E37 J03 L03 P56 X16
IN DUVDEVANI, T; MELMAN, A; PELED, E
PA (UYRA-N) UNIV RAMOT APPLIED RES & IND DEV LTD
CYC 84
PI WO 9944245 A1 19990902 (199945)* EN 35p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9926369 A 19990915 (200004)
EP 1066656 A1 20010110 (200103) EN
R: DE ES FR GB IT NL SE
IL 123419 A 20001206 (200103)
IL 126830 A 20010520 (200153)
KR 2001034536 A 20010425 (200164)

ADT WO 9944245 A1 WO 1999-IL109 19990222; AU 9926369 A AU 1999-26369 19990222; EP 1066656 A1 EP 1999-906424 19990222, WO 1999-IL109 19990222; IL 123419 A IL 1998-123419 19980224; IL 126830 A IL 1998-126830 19981030; KR 2001034536 A KR 2000-709294 20000823

FDT AU 9926369 A Based on WO 9944245; EP 1066656 A1 Based on WO 9944245

PRAI IL 1998-126830 19981030; IL 1998-123419 19980224

AB WO 9944245 A UPAB: 19991103

NOVELTY - The ion conductive matrix comprises 5 - 60 volume percent (vol.%) of inorganic powder in form of sub-micron particles having good aqueous electrolyte absorption capacity, 5 - 50 vol.% of **polymeric** binder compatible with an aqueous electrolyte, and 10 - 90 vol.% of an aqueous electrolyte.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(i) Method for casting membrane which comprises preparing mixture comprising inorganic powder, **polymeric** binder, at least one high boiling point solvent with boiling point above 100 deg. C and at least one low boiling point solvent in which the **polymeric** binder is soluble or forms a gel at casting temperature. Film is casted out of mixture and low boiling point solvent is evaporated from mixture to form solid film. Solid film is washed to replace high boiling point solvent with aqueous electrolyte solution. Alternatively, mixture is heated to its softening temperature and film is formed by hot extrusion of softened mixture. The high boiling point solvent used in the mixture has boiling point above 90 deg. C. Film is cooled to obtain solid film, and washed to replace solvent with aqueous electrolyte solution.

(ii) Method for casting composite electrode comprising steps involved in casting **membrane**. **Alternatively**, preparing composite electrode by extrusion which comprises steps involved in preparing membrane by extrusion.

USE - For forming membranes, composite electrode, electrochemical cell, fuel cell and water electrolizer.

ADVANTAGE - Novel, low cost and highly conductive ion conducting matrix, membranes and electrodes are provided. The ion conducting membranes have good porosity and mechanical properties. Internal lubricants with low solubility in water is used to achieve solubility factor not higher than 14 (cal/cc)1/2, thereby preventing the migration of internal lubricants out of ion conductive membranes when they come in contact with water at washing phase or acid loading phase.

Dwg.0/2

TECH UPTX: 19991103

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Matrix: The ion conducting matrix is a proton conducting matrix and comprises desirably 5 - 50 % of inorganic powder such as silicon dioxide (SiO2), zirconium oxide (ZrO2), boron trioxide (B2O3), titanium oxide (TiO2), aluminum oxide (Al2O3), and/or optional hydroxides or oxy-hydroxides of Ti, Al, B or Zr with a surface area of at least 10 m2/g. The matrix optionally comprises 0.1 - 25 % of nonvolatile liquid lubricant which is compatible with all the components in matrix.

Preferred Electrolyte: The aqueous electrolyte consists of aqueous soluble salt and/or base which is used in aqueous solution having molar

concentration of 0.1 - 10 M, preferably 1 - 5 M.
Alkali metal salts, alkali earth metal salts, R4NX, where
R = organic radical;
X = anion derived from an inorganic acid.
Ammonium chloride (NH4Cl) and/or zinc chloride (ZnCl2) is used as the aqueous soluble salt.
R4NOH, where
R = hydrogen or an organic radical, alkali and/or alkali earth base compound is used as the aqueous soluble bases.
Preferred Membrane: The membrane comprises ion conducting matrix having electronically nonconductive inorganic material with particle size less than 150 nm. The membrane comprises pores with size less than 50 nm. The inorganic powder of matrix is treated with acid or base prior to preparation of membrane. The membrane further comprises electronic nonconductive reinforcing element.
Preferred Electrode: The composite electrode comprises 10 - 70 vol.% of the matrix and remaining electrode material.
Preferred Electrochemical Cell: The electrochemical cell comprises membrane or at least one electrode having electrode material of carbon and/or graphite, metal oxides such as RuO2, WOx or MnO2. Cadmium, zinc, and/or aluminum or its alloys is used as anode active material. Manganese oxide (MnO2), silver oxide or nickel oxy hydroxide (NiOOH) is used as cathode active material. Zn or Al anode and oxygen or air electrode which consists of double layer film with **hydrophobic** air side and **hydrophilic** ionic membrane side is used. The air electrode catalyst is compatible with aqueous solutions of ionic conductive membrane such as oxides of platinum, palladium, gold, silver, copper, manganese, tungsten and/or metal-porphyrin complexes of their salts. The electrochemical cell is single structure unit manufactured by hot pressing the electrodes on both sides of the membrane.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Lubricant: Diesters of aliphatic or aromatic dibasic acids, esters of phosphoric acids, hydrocarbons or synthetic hydrocarbons, silicone oils and/or fluorocarbons is used as the lubricant.
Preferred Acid: The proton conducting matrix comprises 10 - 90 vol.% of an acid such as CF3(CF2)nSO3H, HO3S(CF2)nSO3H, where
n = 0 - 9, especially 0 - 4.
sulfuric acid, hydrochloric acid, hydrobromic acid, phosphoric acid and/or nitric acid. The acid is used in an aqueous solution having a molar concentration of 10 - 99 %, preferably 25 - 99 %.
Preferred Solvent: The high boiling point solvent used for casting or preparing membrane or composite electrode is water soluble solvent. Propylene carbonate, ethylene carbonate, dimethyl phthalate, diethyl phthalate, and/or dibutyl phthalate is used as high boiling point solvent for casting or preparing membrane. Tetrahydrofuran, dimethylether (DME), cyclopentanone, acetone, N-methyl pyrrolidone, dimethylacetamide, methylethylketone, and/or dimethyl-formamide is used as the low boiling point solvent for casting or preparing the membrane. Propylene carbonate, diethyl carbonate, dimethyl carbonate, butyrolactone, methyl isoamyl ketone, cyclohexanone, dialkyl phthalate, and/or glycerol triacetate is used as solvent for casting or preparing composite electrode.

TECHNOLOGY FOCUS - **POLYMERS** - Preferred Binder: Polyvinylidene fluoride, polyvinylidene fluoridehexafluoropropylene, poly(tetrafluoroethylene), poly(methylmethacrylate), polysulfone amide, poly(acrylamide), polyvinyl chloride, poly(acrylonitrile), and/or polyvinyl fluoride is used as the **polymeric** binder.

L14 ANSWER 10 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 1999-468807 [39] WPIDS
DNC C1999-137478
TI Composition for **enhancing transport** through cell **membranes**, particularly for delivery of genes or toxins - comprises transporting agent such as **polymer** that changes structure or properties in response to stimulus..
DC A14 A96 A97 B04 B07 D16
IN CRUM, L A; HOFFMAN, A S; LACKEY, C; MOURAD, P D; MURTHY, N; PORTER, T M; PRESS, O; STAYTON, P; TIRRELL, D; PRESS, O W
PA (UYMA-N) UNIV MASSACHUSETTS; (UNIW) UNIV WASHINGTON; (CRUM-I) CRUM L A; (HOFF-I) HOFFMAN A S; (LACK-I) LACKEY C; (MOUR-I) MOURAD P D; (MURT-I) MURTHY N; (PORT-I) PORTER T M; (PRES-I) PRESS O W; (STAY-I) STAYTON P; (TIRR-I) TIRRELL D
CYC 23
PI WO 9934831 A1 19990715 (199939)* EN 52p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9920261 A1 19990726 (199952)
EP 1044021 A1 20001018 (200053) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2001007666 A1 20010712 (200143)
JP 2002500201 W 20020108 (200206) 62p
ADT WO 9934831 A1 WO 1999-US122 19990105; AU 9920261 A AU 1999-20261 19990105; EP 1044021 A1 EP 1999-900750 19990105, WO 1999-US122 19990105; US 2001007666 A1 Provisional US 1998-70411P 19980105, US 1999-226044 19990105; JP 2002500201 W WO 1999-US122 19990105, JP 2000-527278 19990105
FDT AU 9920261 A Based on WO 9934831; EP 1044021 A1 Based on WO 9934831; JP 2002500201 W Based on WO 9934831
PRAI US 1998-70411P 19980105; US 1999-226044 19990105
AB WO 9934831 A UPAB: 19990928
NOVELTY - Composition for **enhancing transport**, or release, through cell **membranes**, between cells, cell barriers or lipid membranes comprises:
(1) a membrane barrier transporting agent (I) and
(2) system for inducing, or enhancing, effectiveness of (I) for **membrane disruption**.
DETAILED DESCRIPTION - (I) is :
(1) a **polymer** (Ia) that changes structure or properties in response to some stimulus;
(2) a hydrophobic peptide (Ib) that forms pores in cell membranes as a function of change in pH, or
(3) a phospholipid disrupting agent (Ic).
ACTIVITY - None given.
MECHANISM OF ACTION - **Disruption** of cell **membranes**.
USE - The composition is particularly used to improve delivery, to cells, of diagnostic or therapeutic agents, including nucleic acids, proteins, synthetic compounds, metals, radiolabels etc., particularly for gene therapy, e.g. treatment or prevention of restenosis, or toxins such as ricin for killing of target cells. It may also be used to release metabolites or other analytes from cells, for subsequent measurement.
ADVANTAGE - The compositions can be controlled and manipulated externally, by noninvasive methods.
DESCRIPTION OF DRAWING(S) - Graph showing inhibition of cellular protein synthesis by ricin toxin A chain (RTA); poly(propylacrylic acid), PPAAc, and a mixture of the two, showing increased delivery of RTA in presence of the **polymer**.
Dwg.6/7
TECH UPTX: 19990928
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Materials: System (b) may

induce a change in structure of (Ia) and is then an alteration in pH, light, ionic strength, solvent composition, temperature or electric field. Alternatively, (b) comprises ultrasound, an electric field and/or radiation to provide an enhancing effect, particularly ultrasound of frequency 20 kHz to 10 MHz for delivery through the skin. Preferred Composition: This may also include:
(1) a diagnostic or therapeutic agent (especially a cytotoxic compound, nucleoside, nucleotide or nucleic acid, ionically or covalently linked to (I)), particularly where (Ia) is pH sensitive, i.e. responsive at pH 5-6.5, the conditions present in an endosome;
(2) an agent that decreases lysosomal degradation, e.g. an enzyme inhibitor or verapamil;
(3) a polycationic **polymer**, e.g. polylysine or chitosan;
(4) a carrier, e.g. micro- or nano-particles, liposomes, emulsions or lipid vesicles;
(5) an agent that increases endocytosis, e.g. an antibody (which may also serve as targeting agent).
Process: The composition is applied to a suspension of cells, to layers of cells, or to lipid membranes, optionally in conjunction with electrophoresis or iontophoresis.
TECHNOLOGY FOCUS - **POLYMERS** - pH-sensitive **polymers** are graft, block or random **polymers** of acrylic acid or its 1-6C linear, branched or cyclic 2-alpha-alkyl derivatives, acrylate ester/acrylic acid copolymers, or **polymers** containing at least one block of protein or peptide that includes imidazole groups.

L14 ANSWER 11 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-045281 [04] WPIDS
DNC C1999-014190
TI **Enhancing transport** across biological **membrane**
- comprises contacting membrane with **conjugate** containing active agent covalently attached to transport **polymer**.
DC B04
IN ROTHBARD, J B; WENDER, P A
PA (STRD) UNIV LELAND STANFORD JUNIOR
CYC 83
PI WO 9852614 A2 19981126 (199904)* EN 50p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9875938 A 19981211 (199917)
EP 975370 A2 20000202 (200011) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
GB 2341390 A 20000315 (200016)
CZ 9904066 A3 20000517 (200031)
CN 1263473 A 20000816 (200055)
GB 2341390 B 20001108 (200058)
AU 734827 B 20010621 (200141)
KR 2001012809 A 20010226 (200154)
BR 9809138 A 20010828 (200158)
US 6306993 B1 20011023 (200165)
JP 2002502376 W 20020122 (200211) 69p
ADT WO 9852614 A2 WO 1998-US10571 19980521; AU 9875938 A AU 1998-75938 19980521; EP 975370 A2 EP 1998-923711 19980521, WO 1998-US10571 19980521; GB 2341390 A WO 1998-US10571 19980521, GB 1999-23841 19991011; CZ 9904066 A3 WO 1998-US10571 19980521, CZ 1999-4066 19980521; CN 1263473 A CN

1998-807186 19980521; GB 2341390 B WO 1998-US10571 19980521, GB 1999-23841 19991011; AU 734827 B AU 1998-75938 19980521; KR 2001012809 A KR 1999-710772 19991120; BR 9809138 A BR 1998-9138 19980521, WO 1998-US10571 19980521; US 6306993 B1 Provisional US 1997-47345P 19970521, US 1998-83259 19980521; JP 2002502376 W JP 1998-550716 19980521, WO 1998-US10571 19980521

FDT AU 9875938 A Based on WO 9852614; EP 975370 A2 Based on WO 9852614; GB 2341390 A Based on WO 9852614; CZ 9904066 A3 Based on WO 9852614; GB 2341390 B Based on WO 9852614; AU 734827 B Previous Publ. AU 9875938, Based on WO 9852614; BR 9809138 A Based on WO 9852614; JP 2002502376 W Based on WO 9852614

PRAI US 1997-47345P 19970521; US 1998-83259 19980521

AB WO 9852614 A UPAB: 20001117

Enhancing the **transport** of a selected compound across a biological membrane comprises contacting the membrane with a **conjugate** containing a biologically active agent covalently attached to a transport **polymer** so that the contacting promotes the transport of the **conjugate** across the membrane at a greater rate than the transport of the non-**conjugated** biological agent across the membrane. The **polymer** comprises 6-25 subunits, at least 50% of which contain a guanidino or amidino side chain group and the **polymer** contains at least 6 continuous guanidino and/or amidino side chain groups. Also claimed are a composition for delivering a biologically active agent across a biological membrane and an excipient and a combinatorial library of **conjugates**.

The biologically active agent preferably includes small organic compounds e.g. the anticancer taxane, antimicrobial agents (against bacteria or fungi such as yeast), polypeptides e.g. protein antigens, proteins, oligosaccharides, nucleic acids and metal ions. The agent has a molecular weight of < 10 kDa. The agent may be linked to the **polymer** via a linker group, preferably a cleavable linker e.g. a linker group that is cleavable by an enzyme or by solvent-mediated cleavage such as an ester, amide or disulphide group, or it may contain a photocleavable group.

USE - The method is used to transport biologically active agents across biological membranes including eukaryotic and prokaryotic cell membranes. The method may be used to screen **conjugates** for biological activity. The **conjugates** are formed form candidate agents including candidate agents selected from a combinatorial library.

Dwg.0/7

L14 ANSWER 12 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 1998-362918 [31] WPIDS

DNN N1998-283296 DNC C1998-111762

TI Glucose sensor for use in low-oxygen environments, useful e.g. in diabetes - comprises an enzyme-containing membrane made from a semi-interpenetrating **polymer** network which increases oxygen transport to the enzyme.

DC A96 B04 D16 J04 S03

IN BLUBAUGH, E A; BRUNSMAN, A R

PA (IMPL-N) IMPLANTED BIOSYSTEMS INC

CYC 23

PI WO 9827419 A1 19980625 (199831)* EN 29p

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU CA JP SI

AU 9856116 A 19980715 (199846)

EP 948743 A1 19991013 (199947) EN

R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

US 5964993 A 19991012 (199949)

AU 720712 B 20000608 (200035)

JP 2001506365 W 20010515 (200133) 27p
ADT WO 9827419 A1 WO 1997-US23426 19971217; AU 9856116 A AU 1998-56116 19971217; EP 948743 A1 EP 1997-952530 19971217, WO 1997-US23426 19971217; US 5964993 A US 1996-769863 19961219; AU 720712 B AU 1998-56116 19971217; JP 2001506365 W WO 1997-US23426 19971217, JP 1998-527981 19971217
FDT AU 9856116 A Based on WO 9827419; EP 948743 A1 Based on WO 9827419; AU 720712 B Previous Publ. AU 9856116, Based on WO 9827419; JP 2001506365 W Based on WO 9827419
PRAI US 1996-769863 19961219
AB WO 9827419 A UPAB: 19991122
An enzyme-containing membrane comprises a semi-interpenetrating **polymer** network of fibrillated polytetrafluoroethylene and a silicon compound, in which the network is infiltrated with an enzyme. Also claimed are: (1) a membrane system useful in a sensor in which efficient oxygen transport is desired, comprising an outer membrane and an inner membrane which is an enzyme-containing membrane as above, and (2) a glucose sensor comprising: a membrane system with an inner and outer membrane, in which the inner membrane is an enzyme-containing membrane as above, and the outer membrane restricts the flow of glucose into the inner membrane; an electrode capable of oxidising hydrogen peroxide; and in which the inner membrane is in between the outer membrane and the electrode.

The silicon compound is a cross-linked polyorganosiloxane, especially a polydimethylsiloxane. The enzyme is capable of oxidising glucose and generating hydrogen peroxide. It is an oxidase, preferably glucose oxidase, and is immobilised within the network as an enzyme gel. The membrane has porosity of 25-55%, and contains 15-40 vol.% silicon compound. The outer membrane comprises polycarbonate. The inner membrane is as above.

USE - The products are used for measuring glucose levels in low-oxygen environments, in an implantable device, especially useful in diabetes.

ADVANTAGE - The sensor accurately measures glucose levels, even in low-oxygen environments e.g. biological fluids. Oxygen is needed in the reaction involved in the measurement process, and the inner **membrane enhances** the **transport** of oxygen to the site of glucose oxidation.

Dwg.0/3

L14 ANSWER 13 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1990-329157 [44] WPIDS
DNC C1990-142890
TI Prepn. of microporous membrane - from mixt. of **hydrophobic polymer** and **hydrophilic polymer** comprising leaching part of **hydrophilic polymer** from matrix.
DC A14 A26 A88 J01
IN KOENHEN, D M; MULDER, M H; ROESINK, H D W; SMOLDERS, C A; MULDER, M H V
PA (XFLO-N) X-FLOW BV
CYC 17
PI EP 395133 A 19901031 (199044)*
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
NL 8901090 A 19901116 (199049)
CA 2015413 A 19901028 (199104)
JP 02302449 A 19901214 (199105)
US 5076925 A 19911231 (199204)
EP 395133 B1 19950201 (199509) EN 7p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69016491 E 19950316 (199516)
ES 2070263 T3 19950601 (199528)
CA 2015413 C 19970225 (199720)

JP 3196029 B2 20010806 (200147) 4p
ADT EP 395133 A EP 1990-200879 19900410; NL 8901090 A NL 1989-1090 19890428; JP 02302449 A JP 1990-111580 19900426; US 5076925 A US 1990-510070 19900417; EP 395133 B1 EP 1990-200879 19900410; DE 69016491 E DE 1990-616491 19900410, EP 1990-200879 19900410; ES 2070263 T3 EP 1990-200879 19900410; CA 2015413 C CA 1990-2015413 19900425; JP 3196029 B2 JP 1990-111580 19900426
FDT DE 69016491 E Based on EP 395133; ES 2070263 T3 Based on EP 395133; JP 3196029 B2 Previous Publ. JP 02302449
PRAI NL 1989-1090 19890428
AB EP 395133 A UPAB: 19930928
A process for preparing a more or less **hydrophillic** micro porous membrane comprises, i) dissolving a **hydrophobic polymer** and a **hydrophillic polymer** in a suitable solvent or mix of solvents, ii) coagulating in a coagulation bath, iii) removing the so obtained membrane from the coagulation bath, (iv) and subsequently leaching at least a part of the **hydrophilic polymer** from the matrix, v) **alternatively** followed by **hydrophobisation**. The **membrane** formed thus may be in a flat or tubular form or in the form of hollow fibres. Also claimed is a microporous membrane comprising essentially of a **hydrophobic polymer** and a more or less **hydrophillic polymer** , which the latter has been cross-linked and has been fixated in or at the **polymer** matrix. The membrane has pores of 0.0001-5 micron, a heat resistance of up to 250 deg.C a water permeability of up to 8000 l/mz L bar. It also has good chemical resistance and mechanical strength.
USE/ADVANTAGE - The membranes prepd. are suitable for membrane separations, based on particle sizes e.g. ultra-and microfilterations. They can also be used as aeration medium, oxygenerator, bioreactor etc.
0/0

L14 ANSWER 14 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1990-218847 [29] WPIDS
DNN N1990-169835 DNC C1990-094502
TI Modifying surface properties of substrates partic. contact lens - by (hydro)peroxidising using ozone to direct graft copolymerisation. on surface.
DC A14 A35 A96 D22 P42 P81
IN FREEMAN, E M; JANSSEN, R A; MCCRAW, E C
PA (CIBA) CIBA GEIGY AG
CYC 23
PI EP 378511 A 19900718 (199029)*
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
AU 9047936 A 19900719 (199037)
NO 9000098 A 19900806 (199037)
CA 2007552 A 19900713 (199039)
FI 9000136 A 19900714 (199040)
PT 92815 A 19900731 (199041)
JP 02228309 A 19900911 (199042)
US 4968532 A 19901106 (199047)
IL 92983 A 19930818 (199340)
EP 378511 B1 19941102 (199442) EN 9p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69013698 E 19941208 (199503)
ES 2064699 T3 19950201 (199511)
NO 178072 B 19951009 (199545)
IE 65586 B 19951101 (199604)
FI 98631 B 19970415 (199721)
ADT EP 378511 A EP 1990-810005 19900104; JP 02228309 A JP 1990-1633 19900110; US 4968532 A US 1989-297018 19890113; IL 92983 A IL 1990-92983 19900105;

EP 378511 B1 EP 1990-810005 19900104; DE 69013698 E DE 1990-613698 19900104, EP 1990-810005 19900104; ES 2064699 T3 EP 1990-810005 19900104; NO 178072 B NO 1990-98 19900109; IE 65586 B IE 1990-137 19900112; FI 98631 B FI 1990-136 19900110

FDT DE 69013698 E Based on EP 378511; ES 2064699 T3 Based on EP 378511; NO 178072 B Previous Publ. NO 9000098; FI 98631 B Previous Publ. FI 9000136

PRAI US 1989-297018 19890113

AB EP 378511 A UPAB: 19930928

Modifying the surface characteristics of a preformed **polymer** substrate to impart **hydrophilicity**, **hydrophobicity** or other desired properties by graft **polymn**. on the substrate having (hydro)peroxy gps. on the **polymer**, of an ethylenically unsatd. monomer, is claimed. The improvement comprises carrying out the graft **polymn**. on the substrate which is swollen with a liq. before or after ozonation, the monomer being insoluble in the liq. to prevent penetration of the monomer into the interior of the substrate and to direct graft **polymn**. of the monomer to the substrate surface.

Pref. the process is carried out in the presence of a variable metal ion to suppress homoplymsn. of the monomer during grafting, partic a ferrous ion, and the ozonation is carried out in water, air, oxygen, or a perhalogenated hydrocarbon medium (PHM) (pref.).

Also claimed is a modification process where the **polymer** substrate is contacted with a soln. which is or contains a chain transfer agent (CTA) to saturate or swell the **polymer**, the soln. being insoluble in the PHM, then ozonated and the monomer graft **polymn** . on the substrate surface.

USE/ADVANTAGE - The process can be used to modify a contact lens (claimed) or other biomedical device semipermeable membrane, film or fibre, which is modified in respect to **hydrophilicity**, hydro phobicity, optical-, transmission-or bacterial-properties dyeability or tintability, opacity, diffraction differences, wettability, bonding characteristics, oxygen permeability, lubricity and multilayer **membrane** technology (claimed). Desired **alteration** of the surface characteristics is achieved while maintaining substrate structural integrity. @

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L14 ANSWER 15 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 1990-147745 [19] WPIDS

DNN N1990-114484 DNC C1990-064685

TI Membrane for iontophoretic agent delivery device - in which prevents passive release of drug with release of drug controlled by electric current.

DC A96 B07 P33 P34 S05

IN GYORY, J R; HAAK, R P; THEEUWES, F

PA (ALZA) ALZA CORP

CYC 21

PI	WO 9003825	A	19900419 (199019)*	
	RW: AT BE CH DE FR GB LU NL SE			
	W: AU DK FI IT JP KR NO US			
	PT 91890	A	19900430 (199022)	
	AU 8944254	A	19900501 (199029)	
	FI 9101589	A	19910402 (199127)	
	EP 436658	A	19910717 (199129)	
	R: AT BE CH DE FR GB IT LI LU NL SE			
	ES 2019517	A	19910616 (199129)#	
	NO 9101186	A	19910603 (199135)	
	DK 9100594	A	19910403 (199139)	
	US 5080646	A	19920114 (199206)	12p
	US 5147296	A	19920915 (199240)	12p

JP 04505861 W 19921015 (199248) 15p
US 5169382 A 19921208 (199252) 12p
US 5169383 A 19921208 (199252) 14p
AU 9229876 A 19930211 (199313)
US 5232438 A 19930803 (199332) 12p
US 5322502 A 19940621 (199424) 12p
AU 658246 B 19950406 (199522)
CA 1336781 C 19950822 (199540)
CA 1337300 C 19951010 (199548)
KR 9614099 B1 19961014 (199928)
EP 931564 A1 19990728 (199934) EN
R: AT BE CH DE FR GB IT LI LU NL SE
JP 11216192 A 19990810 (199942) 17p
US 5232438 B1 20000229 (200018)

ADT EP 436658 A EP 1989-911931 19891002; US 5080646 A US 1988-252402 19881003; US 5147296 A Div ex US 1988-252402 19881003, US 1991-751276 19910828; JP 04505861 W JP 1989-511045 19881002, WO 1989-US4318 19881002; US 5169382 A Cont of US 1988-252402 19881003, US 1991-648269 19910130; US 5169383 A WO 1989-US4318 19891002, US 1990-571577 19900907; AU 9229876 A AU 1992-29876 19921203, Div ex AU 1989-44254 ; US 5232438 A Cont of US 1988-252402 19881003, Cont of US 1991-648269 19910130, US 1992-898618 19920615; US 5322502 A Cont of US 1988-252402 19881003, Cont of US 1991-648269 19910130, Cont of US 1992-898618 19920615, US 1993-3761 19930113; AU 658246 B AU 1992-29876 19921203, Div ex AU 1989-44254 ; CA 1336781 C Div ex CA 1989-614338 19890928, CA 1994-616939 19941024; CA 1337300 C CA 1989-614338 19890928; KR 9614099 B1 WO 1989-US4318 19891002, KR 1990-701164 19900602; EP 931564 A1 Div ex EP 1989-911931 19891002, EP 1999-201332 19891002; JP 11216192 A Div ex JP 1989-511045 19891002, JP 1998-326831 19891002; US 5232438 B1 Cont of US 1988-252402 19881003, Cont of US 1991-648269 19910130, US 1992-898618 19920615

FDT US 5147296 A Div ex US 5080646; JP 04505861 W Based on WO 9003825; US 5169383 A Based on WO 9003825; US 5232438 A Cont of US 5080646, Cont of US 5169382; US 5322502 A Cont of US 5080646, Cont of US 5169382, Cont of US 5232438; AU 658246 B Previous Publ. AU 9229876; EP 931564 A1 Div ex EP 436658; US 5232438 B1 Cont of US 5080646, Cont of US 5169382

PRAI US 1988-252402 19881003; ES 1989-4346 19891222

AB WO 9003825 A UPAB: 19930928

Membrane for controlling agent delivery from an iontophoretic agent delivery device adapted to deliver the agent through an intact body surface is claimed, the device having a reservoir contg. the agent to be delivered and being connectable to a source of electrical power for driving the agent from the reservoir and through the body surface, in which the membrane is interposed between the agent reservoir and the body surface, the membrane permitting electrically-assisted flux (JEK) of the agent and preventing passive flux (Jp) of the agent, the membrane exhibiting a (JEK + Jp)/Jp ratio of at least 4, a voltage drop across the membrane of less than 1 volt and a Jp of less than 100 microgram/hr-cm2.

The membrane may be formed by dissolving in a solvent, eg CH2Cl2 and CH3OH, 60-95 pts. wt. of cellulose acetate and 5-40 pts. wt. of a water soluble material, eg. polyethylene glycol, having a mol. wt. at least great as the agent mol. wt., casting the membrane, evapg. the solvent and leaching out all of the water soluble material. **Alternatively** the **membrane** may comprise a mixt. of a **hydrophilic** resin, eg. PVP or an ion exchange resin having a functional gp. selected from sulphonic acid, carboxylic acid, imidodiatcetic acid and quaternary amines and **hydrophobic polymer**, eg. an ethylene vinyl acetate **polymer** having a vinyl acetate content of 1-40 wt. Also claimed is a method for testing performance characteristics of an iontophoretic agent delivery device adapted for delivering an agent through an intact body surface, using the membrane.

ADVANTAGE - Using the membrane, the passivee release of drug from the device is prevented and the release of drug is controlled by the magnitude of the electric current. Even if the skin is compromise the amt. of drug delivered ise controlled to a safe level. The membrane can have passive and electrically-assisted transport characteristics similar to that of skin and can be used to test performance characteristics iontophoretic del

L14 ANSWER 16 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1988-292714 [41] WPIDS
DNN N1988-222169 DNC C1988-129791
TI Air treatment device contg. volatile active ingredient - has block of erodable gel cast on membrane with liq partially penetrating membrane during casting.
DC A26 A88 A96 B07 C03 D22 P14 P34
IN SANTINI, T F
PA (DLAI-N) DE LAIRE INC; (DELA-N) DELAIRE INC
CYC 17
PI WO 8807383 A 19881006 (198841)* EN 51p
RW: AT BE CH DE FR GB IT LU NL SE
W: AU BR DK
ZA 8802046 A 19880913 (198849)
AU 8815736 A 19881102 (198904)
US 4809912 A 19890307 (198912) 16p
EP 309549 A 19890405 (198914) EN
R: BE CH DE FR GB IT LI NL
PT 87095 A 19890330 (198916)
ADT WO 8807383 A WO 1988-US1014 19880324; ZA 8802046 A ZA 1988-2046 19880322; US 4809912 A US 1987-32047 19870327; EP 309549 A EP 1988-903665 19880324
PRAI US 1987-32047 19870327
AB WO 8807383 A UPAB: 19930923
An air treatment device has a block of erodible gel enclosed in a vessel whose mouth is closed by a porous membrane. The gel is cast onto the membrane and liquid partially penetrates the membrane so that the solidified gel is physically attached to the membrane which will support the weight of the cast gel.

The membrane is pref. made from **hydrophillic** cellulosic fibres coated with polysiloxane or polydimethylsiloxane. **Alternatively** the **membrane** is a non-woven synthetic textile bonded by a water retarding binder.

USE/ADVANTAGE - The gel has a volatile active ingredient e.g. a fragrance, pheromone, hormone, insecticide, insect attractant, pharmaceutical agent of verterinary drug. The gel is attached to the membrane.

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L14 ANSWER 17 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1987-348651 [49] WPIDS
DNN N1987-261223 DNC C1987-148972
TI Membrane having controlled capillarity - promoting effective contact between cells and the membrane surface, used esp. in a blood-typing device.
DC A96 D16 J04 S03
IN HEWETT, G
PA (GENE-N) GENELABS INC
CYC 15
PI WO 8707304 A 19871203 (198749)* EN 32p
RW: AT BE CH DE FR GB IT LU NL SE
W: AU JP KR
AU 8773957 A 19871222 (198813)
EP 270569 A 19880615 (198824) EN

R: AT BE CH DE FR GB IT LI LU NL SE
JP 01500369 W 19890209 (198912)
US 4851210 A 19890725 (198937) 9p
ADT WO 8707304 A WO 1987-US838 19870414; EP 270569 A EP 1987-903106 19870414; JP 01500369 W JP 1987-502892 19870414; US 4851210 A US 1986-866350 19860522
PRAI US 1986-866350 19860522
AB WO 8707304 A UPAB: 19930922
A structure having controlled capillarity for use in contacting cells in soln. with a membrane comprises (a) a porous membrane surface and (b) a porous interior capable of incorporating the soln. at a controlled rate sufficient to effectively contact the cells with the membrane surface. Pref. the membrane is composed of **polymer** fibres composed of e.g. PVDF, PTFE, modified nylon, nitrocellulose, regenerated cellulose or cellulose.

Absorbent porous materials are modified to produce a material having controlled capillarity through a 2-step process. The first step is to select a base membrane that exhibits a moderately **hydrophilic** character. The second step is the coating of the membrane with chemical agents that control the capillary action of the base membrane materials. One example of such coating agents is **polymers** which make the base membrane slightly more **hydrophobic**. The coating soln. contg. e.g. **polymer**, salt and surfactant is applied after the affinity ligand e.g. antibody, has been bound to the membrane.

USE/ADVANTAGE - The structure has a water-permeable, non-cell **disruptive membrane** that wicks the aqs. phase into a **hydrophilic** matrix thereby efficiently contacting exposed antibodies with cells. The structure is used esp. in a blood typing system and eliminates the possibility of technical or electrical errors. The binding reaction is easily read visibly.

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L14 ANSWER 18 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1987-265616 [38] WPIDS
DNC C1987-112499
TI Cast microporous membrane - formed from a soln. of a pore-forming **polymer** and a film-forming **polymer** and opt. a salt.
DC A18 A28 A32 A96 D16 J01
IN KETRARO, R; LINDER, C; PERRY, M
PA (MEMB-N) MEMBRANE PROD KIRYA
CYC 9
PI EP 238276 A 19870923 (198738)* EN 12p
R: CH DE FR GB IT LI NL
JP 63165111 A 19880708 (198833)
US 4761233 A 19880802 (198833) 11p
ADT EP 238276 A EP 1987-302205 19870316; JP 63165111 A JP 1987-62313 19870317; US 4761233 A US 1987-24327 19870310
PRAI IL 1986-78169 19860317
AB EP 238276 A UPAB: 19930922
Prepn. of a microporous membrane comprises casting the membrane from a soln. comprising (a) a mixt. of at least one pre-forming **polymer** (I) and at least one film-forming **polymer** (II), (b) a solvent for the mixt. of **polymers** and opt. (c) at least one salt, where (I) is one which if cast alone would contract to form either large pores or a non-uniform distribution of material.

Suitable (I) are e.g. halomethylated polyphenyleneoxide, polystyrene derivs., nitrated polysulphones, polyisoprenes and halogenated polysulphones. Suitable (II) are polysulphones, vinylidene fluoride **polymers**, PTFE-based copolymers and polyacry-lonitrile. Suitable salts are LiHCO3, LiCl, MgCl2, MgClO4, ZnCl2, ZnBr2 and ZnI2.

USE/ADVANTAGE - The membranes have well defined surface pore shapes and the pores are larger on the surface and decrease in size to the bottom side of the membrane to allow higher fluxes. The **membranes** are modified easily to **alter** the **hydrophobic/ hydrophilic** balance or are readily charged to increase **hydrophobicity** without redn. in flux. Biologically active components may be crosslinked to prevent dissolution in organic solvents and to minimise copaction under high pressure. Biologically active members can be used as reactors e.g. enzyme membrane reactors or in chromatographic sepn., or in affinity chromatography for removing specific biological species from complex mists.
/3

L14 ANSWER 19 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1986-070217 [11] WPIDS
DNC C1986-029943
TI Sepg. fluid mixt. - by locally heated pervious membrane.
DC J01
IN CHMIEL, H
PA (FRAU) FRAUNHOFER-GES FORD ANGE
CYC 13
PI DE 3518871 A 19860306 (198611)* 13p
WO 8601425 A 19860313 (198612) DE
RW: AT BE CH DE FR GB IT LI NL SE
W: JP US
EP 193570 A 19860910 (198637) DE
R: AT BE CH DE FR GB IT LI LU NL SE
JP 62500289 W 19870205 (198711)
DE 3518871 C 19880511 (198819)
EP 193570 B 19891129 (198948) DE
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3574455 G 19900104 (199003)
US 5089122 A 19920218 (199210)
ADT DE 3518871 A DE 1985-3518871 19850524; WO 8601425 A WO 1985-DE304 19850902; EP 193570 A EP 1985-904424 19850902; JP 62500289 W JP 1985-504004 19850902; US 5089122 A US 1991-649223 19910128
PRAI DE 1984-25754U 19840831; DE 1985-3518871 19850524
AB DE 3518871 A UPAB: 19930922
A multi-component fluid mixt. flows past one face of one or more membranes at whose other face is maintained (e.g. by suction), a lower partial pressure of one of the components than in the mixt., so causing that component to migrate through the membrane, which may be porous (ultrafiltration) or of pervaporation type. The membrane is heated electrically. It may itself be conductive, or carry a conductive coating, or be inductively heated. **Alternatively** the **membrane** is backed by a porous metal support, possibly reinforced by metal netting. The face adjacent the mixt. may be coated with **hydrophobic** or **hydrophilic** material, depending on properties of target substance.
USE/ADVANTAGE - Suitable e.g. for aq. soln.; oil/water mixt.:bio-reaction prod. or for gaseous mixt. Prevents fluid being cooled by loss of evapn. heat, but highly localised effect does not mar main fluid body.
0/3

L14 ANSWER 20 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1968-06690Q [00] WPIDS
TI Desalination using vinyl pyrrolidone copolymer ion.
DC A00
PA (PURQ) PURAQ CO
CYC 1

PI US 3386912 A (196800)*
PRAI US 1965-423976 19650107
AB US 3386912 A UPAB: 19930831
Low energy desalination of sea water by heating to 48 deg.C in that exchanger and passing it to a chamber where it contacts ion-exchange membrane which has a partly water-sol. particulate resin flowing at 50-52 deg.C through chamber. Water is adsorbed by the resin and separated from the **polymer** soln. in settling tank.

Copolymer of a) **hydrophilic** and b) mechanically strengthening **hydrophobic** monomers. a) is vinyl pyrrolidone and b) is vinyl acetate, MMA, chloroprene, acrylonitrile or pref. a mixt. of styrene and butadiene (partic. 60% vinyl pyrrolidone, 20% styrene, 19.5% butadiene and 0.5% cross-linking trialkyl cyanurate moulded between 'Teflon'-coated glass plates 1/32 in apart). **Alternatively** a p.v. pyrrolidone **membrane** coated with an ion-exchange resin may be used.

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FILE 'BIOSIS' ENTERED AT 10:21:13 ON 07 MAR 2002
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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 6 March 2002 (20020306/ED)


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     (FILE 'WPIDS' ENTERED AT 10:07:39 ON 07 MAR 2002)
               DEL HIS Y

     FILE 'BIOSIS' ENTERED AT 10:13:47 ON 07 MAR 2002
L1        772163 S MEMBRANE#
L2         13439 S L1 (4A) (DISRUPT? OR ALTER? OR ENHANC? (3A) (TRANSP? OR PERME
L3        236030 S POLYMER?
L4           262 S L2 AND L3
L5        977182 S TRANSPORT?
L6            45 S L4 AND L5
L7        482259 S MEMBRANE#/IT
L8            25 S L6 AND L7
L9            70 S DISRUPTIVE (3A) AGENT#
L10            1 S L6 AND L9
L11            2 S L1 AND L3 AND L9
L12        20436 S HYDROPHIL?
L13        48724 S HYDROPHOB?
L14            4 S L4 AND L12 AND L13
L15           29 S L8 OR L10 OR L11 OR L14

     FILE 'BIOSIS' ENTERED AT 10:21:13 ON 07 MAR 2002

=> d bib ab it 1-29

L15  ANSWER 1 OF 29  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   2002:161277  BIOSIS
DN   PREV200200161277
TI   PYK2 as a mediator of endothelin-1/Galpha11 signaling to GLUT4 glucose
     transporters.
AU   Park, Jin G.; Bose, Avirup; Leszyk, John; Czech, Michael P. (1)
CS   (1) Program in Molecular Medicine, 373 Plantation St., Worcester, MA,
     01605: Michael.Czech@umassmed.edu USA
SO   Journal of Biological Chemistry, (December 21, 2001) Vol. 276, No. 51, pp.
     47751-47754. http://www.jbc.org/. print.
     ISSN: 0021-9258.
DT   Article
LA   English
AB   Endothelin-1 (ET-1) signaling through Galphaq/11 stimulates translocation
     of intracellular GLUT4 glucose transporters to the plasma
     membrane of 3T3-L1 adipocytes by an unknown mechanism that requires
     protein tyrosine phosphorylation and ADP-ribosylation factor 6 (ARF6) but
     is independent of phosphatidylinositol 3 (PI3)-kinase. In contrast,
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insulin action on this process requires PI3-kinase but not ARF6. Here we report the identification of two proteins selectively tyrosine-phosphorylated in response to ET-1 but not insulin: the Ca2+-activated tyrosine kinase PYK2 and its physiological substrate, the adhesion scaffold protein paxillin. Endogenous paxillin as well as expressed Myc-tagged PYK2 or a Myc-tagged kinase-deficient PYK2 protein were acutely directed to F-actin-rich adhesion sites from the adipocyte cytoplasm in response to ET-1 but not insulin. CADTK-related non-kinase (CRNK) is a dominant negative form of PYK2 containing the C-terminal portion of the protein, which binds paxillin but lacks the PYK2 autophosphorylation site (Tyr402). CRNK expression in 3T3-L1 adipocytes inhibited ET-1-mediated F-actin **polymerization** and translocation of Myc-tagged GLUT4-enhanced green fluorescent protein (EGFP) to the plasma **membrane** without **disrupting** insulin action on these processes. These data reveal the tyrosine kinase PYK2 as a required signaling element in the regulation of GLUT4 recycling in 3T3-L1 adipocytes by ET-1, whereas insulin signaling is directed through a different pathway.

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Endocrine System (Chemical Coordination and Homeostasis)

IT Parts, Structures, & Systems of Organisms
plasma **membranes**

IT Chemicals & Biochemicals
ADP-ribosylation factor 6: analysis, functions, signaling; F-actin: analysis, functions, signaling; GLUT4 glucose **transporters**: analysis, functions; PYK2: analysis, functions; endothelin-1/G-alpha-11: analysis, functions, signaling; enzymes: analysis, functions; green fluorescent protein; insulin: biological activities, functions; kinases: analysis, functions; **membrane** proteins: analysis, functions; paxillin; proteins: analysis, functions; tyrosine: phosphorylation

IT Miscellaneous Descriptors
insulin signalling pathways/mechanisms: analysis, functions

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
3T3-L1 cell line (Muridae)

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

RN 9004-10-8 (INSULIN)
9031-44-1 (KINASES)
57186-25-1 (PAXILLIN)
60-18-4Q (TYROSINE)
556-03-6Q (TYROSINE)

L15 ANSWER 2 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:23609 BIOSIS
DN PREV200200023609
TI Method and composition for **enhancing transport** across biological **membranes**.
AU Rothbard, Jonathan B. (1); Wender, Paul A.
CS (1) Woodside, CA USA
ASSIGNEE: The Board of Trustees of the Leland Stanford, Jr. University, Stanford, CA, USA
PI US 6306993 October 23, 2001
SO Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 23, 2001) Vol. 1251, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.

DT Patent
LA English
AB Methods and compositions for **transporting** drugs and macromolecules across biological membranes are disclosed. In one embodiment, the invention includes a method for enhancing **transport** of a selected compound across a biological membrane, wherein a biological membrane is contacted with a conjugate containing a biologically active agent that is covalently attached to a **transport polymer**. In one embodiment, the **polymer** consists of from 6 to 25 subunits, at least 50% of which contain a guanidino or amidino sidechain moiety. The **polymer** is effective to impart to the attached agent a rate of trans-membrane **transport** across a biological membrane that is greater than the rate of trans-membrane **transport** of the agent in nonconjugated form.
IT Major Concepts
Biochemistry and Molecular Biophysics; **Membranes** (Cell Biology)
IT Chemicals & Biochemicals
compositions; drugs: pharmaceutical, **transport**; macromolecules: **transport**
IT Miscellaneous Descriptors
biological **membranes**

L15 ANSWER 3 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:8763 BIOSIS
DN PREV200200008763
TI Application of surface modified polypropylene membranes to an anaerobic membrane bioreactor.
AU Sainbayar, A. (1); Kim, J. S. (1); Jung, W. J. (1); Lee, Y. S. (1); Lee, C. H. (1)
CS (1) School of Chemical Engineering, Seoul National University, Gwanak-gu, Sillim-dong, Seoul, 151-744 South Korea
SO Environmental Technology, (September, 2001) Vol. 22, No. 9, pp. 1035-1042. print.
ISSN: 0959-3330.
DT Article
LA English
AB In order to increase **hydrophilicity** and thereby to reduce membrane fouling caused by **hydrophobic** adsorption, the surface of a **hydrophobic** 0.2 mum polypropylene (PP) membrane was modified by ozone treatment followed by graft **polymerization** with 2-hydroxy-ethyl methacrylate (HEMA). The modified PP (MPP) membranes were characterized in terms of contact angle, morphology and degree of grafting (DG). The contact angle was reduced from 112degree for a PP membrane to nearly 0degree for MPP membranes by introducing functional groups such as hydroxyl (-OH) and carbonyl groups (C=O) on the membrane surface. As the DG increased, the O/C ratio and membrane resistance of the MPP membrane increased. Using the MPP membrane in the crossflow operation of an anaerobic **membrane** bioreactor (MBR), the **membrane permeability** was **enhanced** although it was largely dependent on the DG of MPP.
IT Major Concepts
Biomaterials; Bioprocess Engineering; Methods and Techniques
IT Chemicals & Biochemicals
2-hydroxy-ethyl methacrylate [HEMA]; carbonyl group; hydroxyl group
IT Methods & Equipment
anaerobic membrane bioreactor: laboratory equipment; crossflow operation: production method; graft **polymerization**: production method; ozone treatment: production method

IT Miscellaneous Descriptors
hydrophilicity; hydrophobic absorption: membrane fouling effect; membrane permeability; polypropylene membrane: application, characterization, contact angle, grafting degree, morphology, surface modified
RN 868-77-9 (2-HYDROXY-ETHYL METHACRYLATE)

L15 ANSWER 4 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:543445 BIOSIS
DN PREV200100543445
TI Phospholipid **alterations** in hepatocyte **membranes** and **transporter** protein changes in cholestatic rat model.
AU Hyogo, Hideyuki; Tazuma, Susumu (1); Nishioka, Tomoji; Ochi, Hidenori; Yamaguchi, Atushi; Numata, Yoshihiro; Kanno, Keishi; Sakomoto, Minoru; Asamoto, Yasumasa; Tsuboi, Kazuhiko; Nakai, Kuniharu; Yasumiba, Shigeyuki; Sunami, Yasushi; Kajiyama, Goro
CS (1) First Department of Internal Medicine, Hiroshima University School of Medicine, 1-2-3 Kasumi, Minami-ku, Hiroshima, 734-8551 Japan
SO Digestive Diseases and Sciences, (October, 2001) Vol. 46, No. 10, pp. 2089-2097. print.
ISSN: 0163-2116.
DT Article
LA English
SL English
AB Biliary components are **transported** by hepatic adenosine triphosphate-binding cassette (ABC) **transporters** that are located in canalicular membranes. Physiological **transporter** function is related to membrane fluidity, which is modulated by the phospholipid composition of the lipid bilayer. We hypothesized that cholestasis may alter **transporter** function by modifying phospholipid species to protect the cell from cholestatic damage. Therefore, we examined the expression of ABC **transport** proteins and their mRNA levels in canalicular membrane vesicles isolated from rat liver 6 hr or three days after bile duct ligation. Membrane lipid composition and membrane fluidity of both sinusoidal and canalicular membrane vesicles were also examined. By 6 hr after bile duct ligation, we found a clear increase of mdr2 and bsep mRNA. These changes were associated with an increase of mdr-Pgp and with a clear decrease of mrp2 protein, and small decrease of bsep protein. In addition, mdr1b mRNA showed a strong increase by three days after bile duct ligation. Canalicular membrane fluidity decreased in a marked time-dependent manner, whereas sinusoidal membranes showed biphasic changes: increased fluidity at 6 hr and a decrease at three days. These changes were closely related to the changes of membrane lipid constitution; the saturated/unsaturated fatty acid ratio increased for phosphatidylcholine in canalicular membrane and the reverse occurred in sinusoidal membrane, and those for sphingomyelin showed the opposite pattern. We conclude that cholestasis causes modulation of ABC **transporters** as well as that of the lipid constitution in lipid bilayer. These may confer cytoprotective resistance to hepatocytes against cholestatic stress.
IT Major Concepts
Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation); **Membranes** (Cell Biology)
IT Parts, Structures, & Systems of Organisms
bile duct: digestive system; hepatocytes: digestive system, **membranes**; liver: digestive system
IT Diseases
cholestasis: digestive system disease, histopathology
IT Chemicals & Biochemicals
ATP-binding cassette **transporters**: expression; besp messenger

RNA; bsep protein; lipid bilayer; mdr1b messenger RNA; mdr2 messenger RNA; **membrane** phospholipids: **alterations**; mrp2 protein; phosphatidylcholine; sphingomyelin; **transporter** proteins

IT Alternate Indexing
Cholestasis (MeSH)

IT Methods & Equipment
Western blot: detection method, gene mapping, labeling; bile duct ligation: surgical method; fluorescence polarization analysis: analytical method; reverse transcriptase-**polymerase** chain reaction: genetic method, **polymerase** chain reaction

IT Miscellaneous Descriptors
membrane fluidity

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rat (Muridae): animal model, strain-Sprague-Dawley

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L15 ANSWER 5 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:48510 BIOSIS
DN PREV200100048510
TI pH-responsive pseudo-peptides for cell **membrane disruption**.
AU Eccleston, M. E.; Kuiper, M.; Gilchrist, F. M.; Slater, N. K. H. (1)
CS (1) Department of Chemical Engineering, University of Cambridge, Pembroke Street, Cambridge, CB2 3RA: nigel_slater@cheng.cam.ac.uk UK
SO Journal of Controlled Release, (3 November, 2000) Vol. 69, No. 2, pp. 297-307. print.
ISSN: 0168-3659.
DT Article
LA English
SL English
AB We describe pseudo-peptides obtained by the copolymerisation of L-lysine and L-lysine ethyl-ester with various **hydrophobic** dicarboxylic acid moieties. In aqueous solution, when the carboxylic acid groups are charged, the **polymers** dissolve. When they are fully neutralised the **hydrophobic** moieties cause the **polymer** to precipitate. The pH range over which reversible precipitation occurs can be adjusted by changing the intramolecular **hydrophilic/hydrophobic** balance, by using a carboxylic acid moiety with a different pKa value or by changing the apparent pKa value of the **polymer** through chemical modifications of the backbone. These bio-degradable materials are well tolerated by a range of mammalian cell lines at physiological pH but display an ability to associate with the outer membranes of these cells, which they rupture to varying degrees at pH 5.5. Relative to the degree of lysis displayed by poly(L-lysine iso-phthalamide), lysis was reduced by partial esterification and increased by replacing the aromatic iso-phthaloyl moiety with a long chain aliphatic dodecyl moiety. Similar behaviour was observed for the pH-dependent rupture of human erythrocytes, where poly(L-lysine dodecanamide) displayed enhanced cell lysis at pH values <7.0 relative to poly(L-lysine iso-phthalamide).

IT Major Concepts
Biochemistry and Molecular Biophysics; Membranes (Cell Biology)

IT Parts, Structures, & Systems of Organisms
erythrocytes: blood and lymphatics

IT Chemicals & Biochemicals

L-lysine; L-lysine ethyl ester; poly(L-lysine dodecanamide)
IT Miscellaneous Descriptors
cell **membrane disruption**
ORGN Super Taxa
Hominidae; Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 56-87-1 (L-LYSINE)
4117-33-3 (L-LYSINE ETHYL ESTER)

L15 ANSWER 6 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:533813 BIOSIS
DN PREV200000533813
TI Membranes for endotoxin removal from dialysate: Considerations on feasibility of commercial ceramic membranes.
AU Bender, Heiko; Pflaenzel, Anne; Saunders, Nicola; Czermak, Peter (1); Catapano, Gerardo; Vienken, Joerg
CS (1) Department KMUB-Biotechnology, University of Applied Sciences, Institute of Biochemical Engineering and Membrane Technology, Wiesenstrasse 14, D-35390, Giessen Germany
SO Artificial Organs, (October, 2000) Vol. 24, No. 10, pp. 826-829. print. ISSN: 0160-564X.
DT Article
LA English
SL English
AB As the quality of water in dialysis fluid varies considerably, dialysate is often contaminated by large amounts of bacteria and endotoxins. Membrane properties and operating pressures are acknowledged to give high-flux dialysis with bicarbonate the bacteriological potential to favor passage of endotoxin fragments from the dialysate into the blood stream. Therefore, a sterile dialysate will have to become a standard. Ultrafiltration across hydrophobic synthetic membranes was shown to remove endotoxins (and their fragments) from dialysis water by the combined effect of filtration and adsorption. However, each module can be used for a limited time only. Ceramic **membranes** may represent an **alternative** to **polymeric membranes** for endotoxin removal. In this article, we tested the capacity of different commercial ceramic membranes with nominal molecular weight cut-off down to 1,000 to retain endotoxins from Ps. aeruginosa. The tested membranes did not generally produce dialysate meeting the Association for the Advancement of Medical Instrumentation standard. When using aluminum-containing membranes, we detected aluminum leaking into the dialysate that could possibly be **transported** into the blood stream.
IT Major Concepts
Biomaterials
IT Chemicals & Biochemicals
Pseudomonas aeuroginosa endotoxin; endotoxin: dialysate removal
IT Miscellaneous Descriptors
blood stream; commercial ceramic **membrane**; dialysis fluid: water quality; hydrophobic synthetic **membrane**; **membrane**: endotoxin removal, operating pressure
ORGN Super Taxa
Pseudomonadaceae: Gram-Negative Aerobic Rods and Cocci, Eubacteria, Bacteria, Microorganisms
ORGN Organism Name
Pseudomonas aeuroginosa (Pseudomonadaceae)
ORGN Organism Superterms

Bacteria; Eubacteria; Microorganisms

L15 ANSWER 7 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:504696 BIOSIS
DN PREV200000504696
TI De novo synthesis of proteinase 3 by cytokine primed circulating human polymorphonuclear neutrophils and mononuclear cells.
AU Zhou, Zhijie; Richard, Carol; Menard, Henri A. (1)
CS (1) Division of Rheumatology, McGill University Health Centre, 1650 Cedar Ave., A6-162.1, Montreal, PQ, H3G 1A4 Canada
SO Journal of Rheumatology, (October, 2000) Vol. 27, No. 10, pp. 2406-2411. print.
ISSN: 0315-162X.
DT Article
LA English
SL English
AB Objective: When polymorphonuclear neutrophils (PMN) and peripheral blood monocytes (PBMC) are stimulated with tumor necrosis factor alpha (TNF-alpha), preexisting granule stored proteinase 3 (PR3) is translocated to the surface of their plasma membrane. We investigated whether PR3 gene reactivation and new PR3 protein production were also features of priming by cytokine. Methods: Normal human PMN and PBMC were isolated and stimulated in vitro with TNF-alpha. They were harvested at different intervals and subjected to total RNA and protein analysis. PR3 mRNA was identified by reverse transcription **polymerase** chain reaction, Northern blot, and sequencing. De novo PR3 synthesis was evaluated by metabolic labeling with (35S) methionine followed by immunoprecipitation using anti-neutrophil cytoplasmic antibodies from serum of patients with active Wegener's granulomatosis and mouse monoclonal anti-native PR3 antibodies. Results: Resting PMN and PBMC do not express PR3 mRNA. During priming, PR3 mRNA appears in PMN at 2 h, peaks at 6 h, and has disappeared at 12 h. By comparison, in primed PBMC, PR3 mRNA appears at 6 h, peaks at 12 h, and disappears at 24 h. Immunoprecipitation of metabolically labeled PR3 revealed new synthesis of PR3 by both cell types, a process that was inhibited by cycloheximide. Conclusion: Primed PMN and PBMC can express PR3 mRNA and synthesize new PR3 protein, providing an **alternative** source to **membrane** PR3. Whether that small amount of inducible PR3 has a primary structure, a localization, or a role different from those of preformed PR3 stored in granules remains to be clarified.
IT Major Concepts
Cell Biology; Immune System (Chemical Coordination and Homeostasis); Blood and Lymphatics (**Transport** and Circulation)
IT Parts, Structures, & Systems of Organisms
peripheral blood monocytes: blood and lymphatics, circulating, cytokine primed, immune system; plasma **membrane**; polymorphonuclear neutrophils: blood and lymphatics, circulating, cytokine primed, immune system
IT Chemicals & Biochemicals
cyclohexamide; proteinase 3: de novo synthesis; tumor necrosis factor alpha
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 128028-50-2 (PROTEINASE 3)

L15 ANSWER 8 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:329357 BIOSIS

DN PREV200000329357
TI Hgt1p, a high affinity glutathione **transporter** from the yeast Saccharomyces cerevisiae.
AU Bourbouloux, Andree; Shahi, Puja; Chakladar, Abhijit; Delrot, Serge; Bachhawat, Anand K. (1)
CS (1) Institute of Microbial Technology, Sector 39-A, Chandigarh, 160 036 India
SO Journal of Biological Chemistry, (May 5, 2000) Vol. 275, No. 18, pp. 13259-13265. print.
ISSN: 0021-9258.
DT Article
LA English
SL English
AB A high affinity glutathione **transporter** has been identified, cloned, and characterized from the yeast Saccharomyces cerevisiae. This **transporter**, Hgt1p, represents the first high affinity glutathione **transporter** to be described from any system so far. The strategy for the identification involved investigating candidate glutathione **transporters** from the yeast genome sequence project followed by genetic and physiological investigations. This approach revealed HGT1 (open reading frame YJL212c) as encoding a high affinity glutathione **transporter**. Yeast strains deleted in HGT1 did not show any detectable plasma **membrane** glutathione **transport**, and hgt1DELTA **disruptants** were non-viable in a glutathione biosynthetic mutant (gsh1DELTA) background. The glutathione repressible **transport** activity observed in wild type cells was also absent in the hgt1DELTA strains. The **transporter** was cloned and kinetic studies indicated that Hgt1p had a high affinity for glutathione (Km = 54 muM)) and was not sensitive to competition by amino acids, dipeptides, or other tripeptides. Significant inhibition was observed, however, with oxidized glutathione and glutathione conjugates. The **transporter** reveals a novel class of **transporters** that has homologues in other yeasts and plants but with no apparent homologues in either Escherichia coli or in higher eukaryotes other than plants.
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Methods and Techniques
IT Parts, Structures, & Systems of Organisms
plasma **membrane**
IT Chemicals & Biochemicals
Hgt1p: high affinity glutathione **transporter**; glutathione **transporters**; Saccharomyces cerevisiae HGT1 gene (Ascomycetes)
IT Methods & Equipment
DNA isolation: Extraction, Isolation, Purification and Separation Techniques, isolation method; PCR [**polymerase** chain reaction]; DNA amplification, DNA amplification method, in-situ recombinant gene expression detection, sequencing techniques; cloning: Recombinant DNA Technology, cloning method; kinetic analysis: activity assays, analytical method; synthesis: Synthetic Techniques, synthetic method; tetrad analysis: Molecular Biology Techniques and Chemical Characterization, analytical method
IT Miscellaneous Descriptors
amino acid sequence
ORGN Super Taxa
Ascomycetes; Fungi, Plantae
ORGN Organism Name
Saccharomyces cerevisiae (Ascomycetes)
ORGN Organism Superterms
Fungi; Microorganisms; Nonvascular Plants; Plants

L15 ANSWER 9 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:279411 BIOSIS
DN PREV200000279411
TI Expression of aquaporin-4 water channels in rat cholangiocytes.
AU Marinelli, Raul A.; Pham, Linh D.; Tietz, Pamela S.; LaRusso, Nicholas F. (1)
CS (1) Center for Basic Research in Digestive Diseases, Mayo Clinic, 200 First Street SW, Rochester, MN, 55905 USA
SO Hepatology, (June, 2000) Vol. 31, No. 6, pp. 1313-1317. print. ISSN: 0270-9139.
DT Article
LA English
SL English
AB We recently reported that secretin induces the exocytic insertion of functional aquaporin-1 water channels (AQP1) into the apical membrane of cholangiocytes and proposed that this was a key process in ductal bile secretion. Because AQP1 is present on the basolateral cholangiocyte membrane in low amounts, we hypothesized that another AQP must be expressed at this domain to facilitate transbasolateral water movement. Thus, we investigated the expression, subcellular localization, possible regulation by secretin, and functional activity of AQP4, a mercury-insensitive water channel expressed in other fluid **transporting** epithelia. Using reverse transcription-**polymerase** chain reaction (RT-PCR) on RNA prepared from purified rat cholangiocytes, we amplified a product of 311 bp that was 100% homologous to the reported AQP4 sequence. RNase protection assay confirmed the presence of an appropriate size transcript for AQP4 in cholangiocytes. Immunoblotting detected a band of approximately 31 kd corresponding to AQP4 in basolateral but not apical membranes of cholangiocytes. Secretin did not **alter** the amount of plasma **membrane** AQP4 but, as expected, induced AQP1 redistribution from intracellular to apical plasma membranes. Functional studies showed that AQP4 accounts for about 15% of total cholangiocyte membrane water permeability. Our results indicate that: (1) cholangiocytes express AQP4 messenger RNA (mRNA) and protein and (2) in contrast to AQP1, which is targeted to the apical cholangiocyte membrane by secretin, AQP4 is constitutively expressed on the basolateral cholangiocyte membrane and is secretin unresponsive. The data suggest that AQP4 facilitates the basolateral **transport** of water in cholangiocytes, a process that could be relevant to ductal bile formation.
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); **Membranes** (Cell Biology); Digestive System (Ingestion and Assimilation)
IT Parts, Structures, & Systems of Organisms
cholangiocyte
IT Chemicals & Biochemicals
RNA; RNase protection assay; aquaporin-4 water channel messenger RNA; aquaporin-4 water channels; secretin
IT Methods & Equipment
immunoblotting; reverse transcriptase-**polymerase** chain reaction
IT Miscellaneous Descriptors
transmembrane water **transport**
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Fischer rat (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;

Rodents; Vertebrates
RN 1393-25-5 (SECRETIN)

L15 ANSWER 10 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:268789 BIOSIS
DN PREV200000268789
TI Phospholipid **alterations** in rat hepatocyte **membranes** in cholestasis and cytoprotective **transporter** protein changes.
AU Hyogo, Hideyuki (1); Tazuma, Susumu; Sakamoto, Minoru; Nakai, Kuniharu; Asamoto, Yasumasa; Tsuboi, Kazuhiko; Yasumiba, Shigeyuki; Sunami, Yasushi; Ochi, Hidenori; Muller, Michael; Kajiyama, Goro
CS (1) Hiroshima Univ, Hiroshima Japan
SO Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 1, pp. AASLD A933. print.
Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May 21-24, 2000 American Gastroenterological Association . ISSN: 0016-5085.
DT Conference
LA English
SL English
IT Major Concepts
Membranes (Cell Biology); Digestive System (Ingestion and Assimilation)
IT Parts, Structures, & Systems of Organisms
hepatocyte **membranes**
IT Diseases
cholestasis; digestive system disease
IT Chemicals & Biochemicals
adenosine-triphosphate-binding cassette; cytoprotective **transporter** protein; phospholipids: alterations
IT Alternate Indexing
Cholestasis (MeSH)
IT Methods & Equipment
RT-PCR [reverse transcriptase-**polymerase** chain reaction]: amplification method, analytical method; Western blotting: analytical method
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L15 ANSWER 11 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:79036 BIOSIS
DN PREV200000079036
TI Functional characterization of mutations in melanocortin-4 receptor associated with human obesity.
AU Ho, Guyu; MacKenzie, Robert G. (1)
CS (1) Dept. of Cell Biology, Parke-Davis Pharmaceutical Research, 2800 Plymouth Rd., Ann Arbor, MI USA
SO Journal of Biological Chemistry, (Dec. 10, 1999) Vol. 274, No. 50, pp. 35816-35822.
ISSN: 0021-9258.
DT Article
LA English

SL English

AB Melanocortin-4 receptor (MC4R) is a G protein-coupled receptor implicated in the regulation of body weight. Genetic studies in humans have identified two frameshift mutations of MC4R associated with a dominantly inherited form of obesity. We have generated and expressed the corresponding MC4R mutants in 293T cells and found that cells transfected with the truncation mutants failed to exhibit agonist binding or responsiveness despite retention of structural motifs potentially sufficient for binding and signaling. Immunofluorescence studies showed that the mutant proteins were expressed and localized in the intracellular compartment but absent from the plasma **membrane**, suggesting that these mutations **disrupted** the proper cellular **transport** of MC4R. Further studies identified a sequence in the cytoplasmic tail of MC4R necessary for the cell surface targeting. We further investigated a possible dominant-negative activity of the mutants on wild-type receptor function. Co-transfection studies showed that the mutants affected neither signaling nor cell surface expression of wild-type MC4R. We also characterized three human sequence variants of MC4R, but these exhibited identical affinities for peptide ligands and identical agonist responsiveness. Thus, unlike the obesity-associated MC4R truncation mutants, the polymorphisms of MC4R are unlikely to be contributors to human obesity.

IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Methods and Techniques

IT Parts, Structures, & Systems of Organisms
plasma **membrane**

IT Diseases
obesity: nutritional disease

IT Chemicals & Biochemicals
G protein; melanocortin-4 receptor

IT Alternate Indexing
Obesity (MeSH)

IT Methods & Equipment
PCR [**polymerase** chain reaction]: DNA amplification, DNA amplification method, in-situ recombinant gene expression detection, sequencing techniques; adenylate cyclase assay: Analysis/Characterization Techniques: CB, analytical method; cAMP iodine-125 scintillation proximity assay system: Amersham Pharmacia Biotech, laboratory equipment; cell culture: Cell Culture Techniques, cell culture method; cloning: Recombinant DNA Technology, cloning method; confocal laser scanning microscope: Olympus, laboratory equipment; immunofluorescence: microscopy method, microscopy: CB; oligonucleotide-directed mutagenesis: genetic method, mutagenesis, protein engineering; receptor binding assay: analytical method, binding assays; transfection: gene expression/vector techniques, genetic method

IT Miscellaneous Descriptors
body weight; frameshift mutation; gene polymorphism

ORGN Super Taxa
Cercopithecidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
293T cell line (Hominidae); COS-7 cell line (Cercopithecidae); human (Hominidae)

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Primates; Nonhuman Vertebrates; Primates; Vertebrates

L15 ANSWER 12 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:49083 BIOSIS

DN PREV200000049083
TI Cytosolic delivery of granzyme B by bacterial toxins: Evidence that endosomal disruption, in addition to transmembrane pore formation, is an important function of perforin.
AU Browne, Kylie A.; Blink, Elizabeth; Sutton, Vivien R.; Froelich, Christopher J.; Jans, David A.; Trapani, Joseph A. (1)
CS (1) Austin Research Institute, Studley Road, Heidelberg, VIC Australia
SO Molecular and Cellular Biology, (Dec., 1999) Vol. 19, No. 12, pp. 8604-8615.
ISSN: 0270-7306.
DT Article
LA English
SL English
AB Granule-mediated cell killing by cytotoxic lymphocytes requires the combined actions of a membranolytic protein, perforin, and granule-associated granzymes, but the mechanism by which they jointly kill cells is poorly understood. We have tested a series of **membrane-disruptive agents** including bacterial pore-forming toxins and hemolytic complement for their ability to replace perforin in facilitating granzyme B-mediated cell death. As with perforin, low concentrations of streptolysin O and pneumolysin (causing <10% 51Cr release) permitted granzyme B-dependent apoptosis of Jurkat and Yac-1 cells, but staphylococcal alpha-toxin and complement were ineffective, regardless of concentration. The ensuing nuclear apoptotic damage was caspase dependent and included cleavage of poly(ADP-ribose) **polymerase**, suggesting a mode of action similar to that of perforin. The plasma **membrane** lesions formed at low dose by perforin, pneumolysin, and streptolysin did not permit diffusion of fluorescein-labeled proteins as small as 8 kDa into the cell, indicating that large **membrane** defects are not necessary for granzymes (32 to 65 kDa) to enter the cytosol and induce apoptosis. The endosomolytic toxin, listeriolysin O, also effected granzyme B-mediated cell death at concentrations which produced no appreciable cell **membrane** damage. Cells pretreated with inhibitors of endosomal trafficking such as brefeldin A took up granzyme B normally but demonstrated seriously impaired nuclear targeting of granzyme B when perforin was also added, indicating that an important role of perforin is to disrupt vesicular protein trafficking. Surprisingly, cells exposed to granzyme B with perforin concentrations that produced nearly maximal 51Cr release (1,600 U/ml) also underwent apoptosis despite excluding a 8-kDa fluorescein-labeled protein marker. Only at concentrations of >4,000 U/ml were perforin pores demonstrably large enough to account for transmembrane diffusion of granzyme B. We conclude that pore formation may allow granzyme B direct cytosolic access only when perforin is delivered at very high concentrations, while perforin's ability to disrupt endosomal trafficking may be crucial when it is present at lower concentrations or in killing cells that efficiently repair perforin pores.
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); **Membranes** (Cell Biology); Toxicology
IT Parts, Structures, & Systems of Organisms
endosome; plasma **membrane**: pore
IT Chemicals & Biochemicals
granzyme B; listeriolysin: toxin; perforin; pneumolysin; staphylococcal alpha-toxin; streptolysin O
IT Miscellaneous Descriptors
apoptosis
ORGN Super Taxa
Bacteria: Microorganisms; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata,

Animalia
ORGN Organism Name
Jurkat cell line (Hominidae); Yac-1 cell line (Muridae); bacteria (Bacteria)
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Humans; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
RN 143180-74-9 (GRANZYME B)

L15 ANSWER 13 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:9745 BIOSIS
DN PREV200000009745
TI The design and synthesis of **polymers** for eukaryotic **membrane disruption.**
AU Murthy, Niren; Robichaud, John R.; Tirrell, David A.; Stayton, Patrick S.; Hoffman, Allan S. (1)
CS (1) Department of Bioengineering, University of Washington, Seattle, WA, 98195 USA
SO Journal of Controlled Release, (Aug. 27, 1999) Vol. 61, No. 1-2, pp. 137-143.
ISSN: 0168-3659.
DT Article
LA English
SL English
AB The intracellular trafficking of drugs is critical to the efficacy of drugs that are susceptible to attack by lysosomal enzymes. It is therefore an important goal to design and synthesize molecules which can enhance the **transport** of endocytosed drugs from the endosomal compartments to the cytoplasm. The pH of an endosome is lower than that of the cytosol by one to two pH units, depending on the stage of endosomal development. This pH gradient is a key factor in the design of **membrane-disruptive polymers** which could enhance the endosomal release of drugs. Such **polymers** should **disrupt** lipid bilayer **membranes** at pH 6.5 and below, but should be non-lytic at pH 7.4. We have designed and synthesized pH-sensitive synthetic **polymers** which efficiently disrupt red blood cells within a sharply defined pH range. One of these **polymers**, poly(ethyl acrylic acid) (PEAAc) has been previously shown to disrupt synthetic vesicles in a pH-dependent fashion (6). PEAAc hemolyzes red blood cells with an activity of 107 molecules per red blood cell, which is as efficient on a molar basis as the peptide melittin. The mechanism of RBC hemolysis by PEAAc is consistent with the colloid osmotic mechanism. PEAAc's hemolytic activity rises rapidly as the pH decreases from 6.3 to 5.0, and there is no hemolytic activity at pH 7.4. A related **polymer**, poly(propyl acrylic acid) (PPAAc), was synthesized to test whether making the pendant alkyl group more hydrophobic by adding one methylene group would increase the hemolytic activity. PPAAc was found to disrupt red blood cells 15 times more efficiently than PEAAc at pH 6.1. PPAAc was also not active at pH 7.4 and displayed a pH-dependent hemolysis that was shifted toward higher pH's. Random 1:1 copolymers of ethyl acrylate (EA) and acrylic acid (AAc) (which contain random -COOH and -C2H5 groups that are present and regularly repeat in PEAAc) also displayed significant hemolytic activity, with an efficiency close to PEAAc. These results demonstrate that pH-sensitive synthetic **polymers** can be molecularly engineered to efficiently **disrupt** eukaryotic **membranes** within defined and narrow pH ranges. Thus, these **polymers** might serve as endosomal **disruptive agents** with specificities for early or late endosomes.
IT Major Concepts

Membranes (Cell Biology); Pharmacology
IT Parts, Structures, & Systems of Organisms
endosome; red blood cell: blood and lymphatics; red cell **membrane: disruption**
IT Chemicals & Biochemicals
melittin; poly(ethyl acrylic acid); poly(propyl acrylic acid)
IT Miscellaneous Descriptors
drug delivery; pH
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Hymenoptera: Insecta, Arthropoda, Invertebrata, Animalia
ORGN Organism Name
bee (Hymenoptera); human (Hominidae)
ORGN Organism Superterms
Animals; Arthropods; Chordates; Humans; Insects; Invertebrates; Mammals; Primates; Vertebrates
RN 20449-79-0Q (MELITTIN)
37231-28-0Q (MELITTIN)

L15 ANSWER 14 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:112240 BIOSIS
DN PREV199900112240
TI **Alterations** in adhesion, **transport**, and **membrane** characteristics in an adhesion-deficient pseudomonad.
AU Deflaun, M. F.; Oppenheimer, S. R.; Streger, S.; Condee, C. W.; Fletcher, M. (1)
CS (1) Belle W. Baruch Inst. Marine Biol. Coastal Res., Univ. South Carolina, Columbia, SC 29208 USA
SO Applied and Environmental Microbiology, (Feb., 1999) Vol. 65, No. 2, pp. 759-765.
ISSN: 0099-2240.
DT Article
LA English
AB A stable adhesion-deficient mutant of Burkholderia cepacia G4, a soil pseudomonad, was selected in a sand column assay. This mutant (ENV435) was compared to the wild-type strain by examining the adhesion of the organisms to silica sand and their **transport** through two aquifer sediments that differed in their sand, silt, and clay contents. We compared the longitudinal **transport** of the wild type and the adhesion mutant to the **transport** of a conservative chloride tracer in 25-cm-long glass columns. The **transport** of the wild-type strain was severely retarded compared to the **transport** of the conservative tracer in a variety of aquifer sediments, while the adhesion mutant and the conservative tracer traveled at similar rates. An intact sediment core study produced similar results; ENV435 was **transported** at a faster rate and in much greater numbers than G4. The results of hydrophobic interaction chromatography revealed that G4 was significantly more hydrophobic than ENV435, and polyacrylamide gel electrophoresis revealed significant differences in the lipopolysaccharide O-antigens of the adhesion mutant and the wild type. Differences in this cell surface **polymer** may explain the decreased adhesion of strain ENV435.
IT Major Concepts
Cell Biology; Pollution Assessment Control and Management
IT Parts, Structures, & Systems of Organisms
cell **membranes**: characteristics
IT Chemicals & Biochemicals
cell surface **polymers**; O antigens
IT Miscellaneous Descriptors
adhesion-defective mutants; aquifer sediments; bacterial adhesion

alterations; **transport**; **transport** rates
ORGN Super Taxa
Pseudomonadaceae: Gram-Negative Aerobic Rods and Cocci, Eubacteria, Bacteria, Microorganisms
ORGN Organism Name
pseudomonads (Pseudomonadaceae); Burkholderia cepacia (Pseudomonadaceae): strain-G4
ORGN Organism Superterms
Bacteria; Eubacteria; Microorganisms

L15 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:428583 BIOSIS
DN PREV199800428583
TI Active platelet movements on **hydrophobic/hydrophilic** microdomain-structured surfaces.
AU Ito, Etsuko; Suzuki, Ken; Yamato, Masayuki; Yokoyama, Masayuki; Sakurai, Yasuhisa; Okano, Teruo (1)
CS (1) Inst. Biomed. Eng., Tokyo Women's Med. Univ., 801 Kawada-cho, Shinjuku-ku, Tokyo 162-8666 Japan
SO Journal of Biomedical Materials Research, (Oct., 1998) Vol. 42, No. 1, pp. 148-155.
ISSN: 0021-9304.
DT Article
LA English
AB The early motion and interaction of platelets on a microdomain-structured block copolymer surface composed of 2-hydroxyethyl methacrylate (HEMA)-styrene were analyzed and compared with those on a compositionally identical random copolymer, homopolymer poly (HEMA) (**hydrophilic**) and polystyrene (**hydrophobic**) surfaces. Contacting platelets were quantitatively more active, with motions including rolling, detachment, oscillatory vibration, and change of direction only on the HEMA-St block copolymer surface. Active platelet movements were observed for long time periods (>20 min) on HEMA-St block copolymer surfaces and were distinct from those for inert PSt latex particles on these same surfaces, demonstrating that platelet movements were not due to physical forces such as convection, **hydrophobic** interactions, or microbrownian movement. To study the cause and mechanism underlying the platelet movements, platelets treated with an adenosine triphosphate (ATP) synthesis inhibition, NaN3, or a **membrane** skeleton-**disrupting** chemical agent, dibucaine, were also studied on these surfaces. Both treatments reduced platelet movement and demonstrated that platelets in contact with the HEMA-St block copolymer surface require metabolic processes consuming ATP and involve dynamics of their membrane skeleton. These energy-consuming active movements might explain the previously observed lower platelet activation and low thrombogenicity of the HEMA-St block copolymers. Enhanced platelet movements on the HEMA-St block copolymer surface show that the microdomain surface interacts uniquely with platelets to hinder activation and preserve passive platelet function despite surface contact.
IT Major Concepts
Biomaterials; Blood and Lymphatics (**Transport** and Circulation)
IT Chemicals & Biochemicals
hydrophobic-hydrophilic microdomain-structured surfaces; poly(2-hydroxyethyl methacrylate); polystyrene; ATP; 2-hydroxyethyl methacrylate-styrene copolymer
IT Miscellaneous Descriptors
active platelet movements; blood-**polymer** interaction; **membrane** skeleton dynamics; platelet activation inhibition
RN 25249-16-5 (POLY(2-HYDROXYETHYL METHACRYLATE))

9003-53-6 (POLYSTYRENE)
56-65-5Q (ATP)
42530-29-0Q (ATP)
94587-45-8Q (ATP)
111839-44-2Q (ATP)

L15 ANSWER 16 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:387929 BIOSIS
DN PREV199800387929
TI Renal Na+,K+-ATPase in SHR: Studies of activity and gene expression.
AU Nguyen, A.-T. (1); Hayward-Lester, A.; Sabatini, S.; Doris, P. A.
CS (1) Inst. Mol. Med., Univ. Tex. Health Sci. Cent., 2121 W. Holcombe Blvd., Houston, TX 77030 USA
SO Clinical and Experimental Hypertension, (July-Aug., 1998) Vol. 20, No. 5-6, pp. 641-656.
ISSN: 1064-1963.
DT Article
LA English
AB The mechanism by which increased dietary intake of calcium reduces blood pressure in the spontaneously hypertensive rat is unknown. The present studies were designed to determine if there were alterations in the activity of the major membrane ion translocating pump, sodium, potassium-ATPase (NKA), in the kidneys of hypertensive rats and whether increased dietary calcium intake affected the activity of this enzyme. Fifteen-week old SHR's were found to have lower total ATPase activity in microsomal preparations from the kidney than age matched Wistar-Kyoto animals. Both the ouabain-sensitive component (NKA) and the ouabain-insensitive component were lower in SHR. Increasing dietary calcium intake from 1% to 3% elevated both components of the ATPase activity in SHR, but was without effect in WKY. Measurement of **membrane** phospholipid composition suggested that **altered** phospholipid composition did not account for the reduced ATPase activity observed, but indicated a reduced density of ATPase in SHR. A technique has been devised for qualitative and quantitative analysis of Na, K-ATPase alpha isoforms using RT-PCR. This technique reveals that the alpha I isoform is the sole catalytic isoform present in the nephron. Accurate and precise quantification of the amount of gene expression in individual nephron segments is reported and will be applied to determine whether dietary calcium influences blood pressure by a mechanism which alters nephron NKA gene expression.
IT Major Concepts
Cardiovascular System (**Transport** and Circulation); Enzymology (Biochemistry and Molecular Biophysics); Nutrition; Urinary System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
kidney: excretory system; nephron: excretory system
IT Diseases
hypertension: vascular disease
IT Chemicals & Biochemicals
calcium: dietary intake; potassium-potassium-ATPase: activity, alpha-1 isoform, **membrane** ion translocating pump, renal, gene expression
IT Methods & Equipment
RT-PCR [reverse transcriptase-**polymerase** chain reaction]: analytical method
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae): strain-Wistar-Kyoto, strain-spontaneously hypertensive, weanling

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 9000-83-3 (ATPASE)

L15 ANSWER 17 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:29918 BIOSIS
DN PREV199800029918
TI Regulation of phagosomal acidification. Differential targeting of Na+/H+ exchangers, Na+/K+-ATPases, and vacuolar-type H+-ATPases.
AU Hackam, David J.; Rotstein, Ori D.; Zhang, Wei-Jian; Demaurex, Nicolas; Woodside, Michael; Tsai, Olivia; Grinstein, Sergio (1)
CS (1) Division Cell Biol., Hosp. Sick Children, 555 University Ave., Toronto, ON M5G 1X8 Canada
SO Journal of Biological Chemistry, (Nov. 21, 1997) Vol. 272, No. 47, pp. 29810-29820.
ISSN: 0021-9258.
DT Article
LA English
AB Vacuolar-type (V) ATPases are thought to be the main determinant of phagosomal acidification. In phagosomes containing mycobacteria, which ostensibly impair the delivery of V-ATPases to the phagosomal membrane, the pH would be expected to be near neutral. This prediction was tested by microfluorescence ratio imaging using macrophages from mice susceptible to mycobacterial infection. Although less acidic than their counterparts containing dead bacteria, phagosomes containing live Mycobacteria bovis were nearly 1 pH unit more acidic than the cytosol, suggesting the existence of alternate H+ **transport** mechanisms. We therefore investigated whether Na+/H+ exchange (NHE) contributes to phagosomal acidification. Immunoblotting, reverse transcriptase-**polymerase** chain reaction, and pharmacological studies indicated that NHE1 is the predominant isoform of the exchanger in macrophages. Fractionation revealed that NHE1 is incorporated into the phagosomal membrane, and measurements of pH indicated that it is functional in this location. Nevertheless, acidification of the lumen of phagosomes containing either latex beads or live M. bovis was insensitive to (3-methylsulfonyl-4-piperidinobenzoyl)-guanidine methanesulfonate, a potent inhibitor of NHE 1. This may have been due to the absence of an appropriate lumen to cytosol Na+ gradient, because the phagosomal membrane was found to be devoid of Na+/K+ pumps. Unexpectedly, the acidification of M. bovis phagosomes was fully reversed by specific inhibitors of the vacuolar H+ATPase, suggesting that ATPases are present only transiently or in reduced quantities in the phagosomal **membrane**. **Alternatively**, acid equivalents accumulated in endosomes by V-ATPases may be delivered to the mycobacterial phagosome by carrier vesicles devoid of ATPases.
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Infection; **Membranes** (Cell Biology)
IT Parts, Structures, & Systems of Organisms
macrophage: immune system; phagosome: acidification, **membrane**
IT Diseases
Mycobacterium-bovis infection: bacterial disease
IT Chemicals & Biochemicals
sodium/hydrogen exchanger; sodium/potassium ATPase; vacuolar-type hydrogen ATPase
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Mycobacteriaceae: Mycobacteria, Actinomycetes and Related Organisms, Eubacteria, Bacteria, Microorganisms

ORGN Organism Name
mouse (Muridae): host; J774 (Muridae); Mycobacterium-bovis (Mycobacteriaceae): pathogen
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 9000-83-3 (ATPASE)

L15 ANSWER 18 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:482937 BIOSIS
DN PREV199799782140
TI The apoptosis-necrosis paradox: Apoptogenic proteases activated after mitochondrial permeability transition determine the mode of cell death.
AU Hirsch, Tamara; Marchetti, Philippe; Susin, Santos A.; Dallaporta, Bruno; Zamzami, Naoufal; Marzo, Isabel; Geuskens, Maurice; Kroemer, Guido
CS Centre Natl. Rech. Sci., Unite Propre Recherche 420, 19 rue Guy Moquet, F-94801 Villejuif France
SO Oncogene, (1997) Vol. 15, No. 13, pp. 1573-1581.
ISSN: 0950-9232.
DT Article
LA English
AB Mitochondrial alterations including permeability transition (PT) constitute critical events of the apoptotic cascade and are under the control of Bcl-2 related gene products. Here we show that induction of PT is sufficient to activate CPP32-like proteases with DEVDase activity and the associated cleavage of the nuclear DEVDase substrate poly(ADP-ribose) **polymerase** (PARP). Thus, direct intervention on mitochondria using a ligand of the mitochondrial benzodiazepin receptor or a protonophore causes DEVDase activation. In addition, the DEVDase activation triggered by conventional apoptosis inducers (glucocorticoids or topoisomerase inhibitors) is prevented by inhibitors of PT. The protease inhibitor N-benzyloxycabonyl-Val-Ala-Asp-fluoromethylketone (Z-VAD.fmk) completely prevents the activation of DEVDase and PARP cleavage, as well as the manifestation of nuclear apoptosis (chromatin condensation, DNA fragmentation, hypoploidy). In addition, Z-VAD.fmk delays the manifestation of apoptosis-associated changes in cellular redox potentials (hypergeneration of superoxide anion, oxidation of compounds of the inner mitochondrial membrane, depletion of non-oxidized glutathione), as well as the exposure of phosphatidylserine residues in the outer plasma membrane leaflet. Although Z-VAD.fmk retards cytolysis, it is incapable of preventing **disruption** of the plasma **membrane** during protracted cell culture (12-24 h), even in conditions in which it completely blocks nuclear apoptosis (chromatin condensation and DNA fragmentation). Electron microscopic analysis confirms that cells treated with PT inducers alone undergo apoptosis, whereas cells kept in identical conditions in the presence of Z-VAD.fmk die from necrosis. These observations are compatible with the hypothesis that PT would be a rate limiting step in both the apoptotic and the necrotic modes of cell death. In contrast, it would be the availability of apoptogenic proteases that would determine the choice between the two death modalities.
IT Major Concepts
Blood and Lymphatics (**Transport** and Circulation); Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Genetics; **Membranes** (Cell Biology); Metabolism
IT Chemicals & Biochemicals
PROTEASES; PROTEASE
IT Miscellaneous Descriptors
ANIMAL MODEL; APOPTOGENIC PROTEASE ACTIVATION; APOPTOSIS-NECROSIS PARADOX; CELL BIOLOGY; CELL DEATH MODE; ENDOCRINE SYSTEM; IMMUNE

SYSTEM; IN-VITRO MODEL SYSTEM; MITOCHONDRIAL PERMEABILITY TRANSITION; MOLECULAR GENETICS; THYMOCYTES
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Balb/C mouse (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN 9014-01-1 (PROTEASES)
9001-92-7 (PROTEASE)

L15 ANSWER 19 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:463912 BIOSIS
DN PREV199799763115
TI Synthetically modified cellulose: An **alternative** to synthetic **membranes** for use in haemodialysis.
AU Hoenich, Nicholas A. (1); Woffindin, Celia; Stamp, Susan; Roberts, Sarah J.; Turnbull, Jean
CS (1) Dep. Med., Sch. Clin. Med. Sci., Floor 4, William Leech Build., Med. Sch., Univ. Newcastle, Framlington Place, Newcastle upon Tyne NE2 4HH UK
SO Biomaterials, (1997) Vol. 18, No. 19, pp. 1299-1303.
ISSN: 0142-9612.
DT Article
LA English
AB Renal replacement therapy relies predominantly on the use of cellulose-based membranes. Such membranes have a biocompatibility profile which is inferior to membranes manufactured from synthetic **polymers**. Synthetically modified cellulose (SMC) is a new, low-flux haemodialysis membrane in which hydroxyl groups have been replaced with benzyl groups. The biocompatibility profile characterized by changes in white cell and platelet counts and the activation of complement components (C3a, C5a and C5b-9) have been studied in vivo and compared with those of cellulose acetate, unmodified cellulose (Cuprophan) and low-flux polysulphone (Fresenius Polysulfone) in the same group of patients. For SMC, the white cell count at 15 min declined to 65.6% of pretreatment level, compared with 63.8% for the cellulose acetate, 79.6% for low-flux polysulphone and 28.1% for Cuprophan, thereafter returning to pretreatment levels. Both modified cellulose membranes were superior to unmodified cellulose (P = 0.001); the differences between the modified cellulose membranes were not significant statistically. The changes induced by all three cellulose-based membranes exceeded those for low-flux polysulphone (P = 0.001). Associated with the neutropenia was a reduction in platelet count, but this was independent of membrane type. The mean time-averaged concentrations of C3-des Arg over 150 min were 1168 ng ml-1 (SMC), 1030 ng ml-1 (cellulose acetate), 1297 ng ml-1 (Cuprophan) and 790 ng ml-1 (low-flux polysulphone). Equivalent values for C5-des Arg were 6.12 (SMC), 2.98 (cellulose acetate), 11.03 (Cuprophan) and 1.33 ng ml-1 (low-flux polysulphone). C5b-9 values were 385 (SMC), 386 (cellulose acetate), 177 (Cuprophan) and 185 ng ml-1 (low-flux polysulphone). For each of the complement components the differences between the membranes were significant (P = 0.0009 (C3a-des Arg), P = 0.0001 (c5a-des Arg and C5b-9)). The levels of C5b-9 generated during dialysis also showed a significant positive correlation compared to C5a for all membranes considered as a single group (Pearson's correlation coefficient = 0.870, P = 0.0001). It is concluded that the modification of the cellobiosic unit is a promising approach to improve the biocompatibility profile of cellulose-based membranes. The two different methods of modification lead to similar improvements in biocompatibility compared with unmodified cellulose, but as yet do not match that of low-flux polysulphone.

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (**Transport** and Circulation); General Life Studies; Immune System (Chemical Coordination and Homeostasis); Methods and Techniques; Pathology; Urinary System (Chemical Coordination and Homeostasis)
IT Chemicals & Biochemicals
CELLULOSE
IT Miscellaneous Descriptors
BIOBUSINESS; BIOCHEMISTRY AND BIOPHYSICS; BIOMATERIALS; CELLULOSE; COMPLEMENT; COMPLEMENT ACTIVATION; HEMODIALYSIS; MEDICAL RESEARCH; METHODOLOGY; PATIENT; RENAL REPLACEMENT THERAPY; SYNTHETIC **MEMBRANE ALTERNATIVES**; SYNTHETICALLY MODIFIED; THERAPEUTIC METHOD
ORGN Super Taxa
Hominidae; Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 9004-34-6 (CELLULOSE)

L15 ANSWER 20 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:435991 BIOSIS
DN PREV199799735194
TI The major intrinsic protein family of arabidopsis has 23 members that form three distinct groups with functional aquaporins in each group.
AU Weig, Alfons; Deswarte, Corine; Chrispeels, Maarten J. (1)
CS (1) Dep. Biol., 0116, University Calif. San Diego, 9500 Gilman Dr., La Jolla, CA 92093-0116 USA
SO Plant Physiology (Rockville), (1997) Vol. 114, No. 4, pp. 1347-1357. ISSN: 0032-0889.
DT Article
LA English
AB Aquaporins, proteins that **enhance** the **permeability** of biological **membranes** to water, are widely distributed in living organisms. They are 26- to 29-kD proteins that belong to the major intrinsic protein (MIP) family of channels. By searching the Arabidopsis thaliana expressed sequence tag database and by using the **polymerase** chain reaction with oligonucleotides to conserved plant aquaporin domains, we identified 23 expressed Arabidopsis MIP genes. Eight of these had been previously identified as active aquaporins, and two additional ones are now reported to have water-**transport** activity in Xenopus laevis oocytes. One of these is highly expressed in suspension-cultured cells. On a dendrogram these 23 MIP sequences cluster into three groups: the first group has 11 members and contains the plasma membrane aquaporins, the second group also has 11 members and contains the tonoplast aquaporins, and the third group has only a single member. This MIP protein, provisionally called At-NLM1, is most closely related to the Gm-NOD26 protein that is found in the bacteroid membranes of soybean (Glycine max L.) nodules; At-NLM1 is an active aquaporin when expressed in oocytes. With a semiquantitative slot-blot analysis technique, we determined the expression levels of 22 MIP genes in the various organs. The quantitative **polymerase** chain reaction was used to determine the effects of various stress treatments on the expression of NLM1.
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Genetics; **Membranes** (Cell Biology)
IT Miscellaneous Descriptors
AQUAPORINS; BIOCHEMISTRY AND BIOPHYSICS; GENETIC METHOD; MAJOR INTRINSIC PROTEIN GENES; **MEMBRANE** PROTEINS; **MEMBRANES**

; MIP GENES; MOLECULAR GENETICS; QUANTITATIVE **POLYMERASE** CHAIN REACTION REACTION; WATER-SELECTIVE CHANNELS

ORGN Super Taxa
Cruciferae; Dicotyledones, Angiospermae, Spermatophyta, Plantae; Leguminosae; Dicotyledones, Angiospermae, Spermatophyta, Plantae

ORGN Organism Name
Arabidopsis thaliana (Cruciferae); Glycine max (Leguminosae)

ORGN Organism Superterms
angiosperms; dicots; plants; spermatophytes; vascular plants

L15 ANSWER 21 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:409938 BIOSIS
DN PREV199799701981
TI G-protein-mediated signaling in cholesterol-enriched arterial smooth muscle cells. 1. Reduced membrane-associated G-protein content due to diminished isoprenylation of G-gamma subunits and p21ras.
AU Pomerantz, Kenneth B.; Lander, Harry M.; Summers, Barbara; Robishaw, Janet D.; Balcueva, Eric; Hajjar, David P. (1)
CS (1) Dep. Med. Biochem., Cornell Univ. Med. Coll., 1300 York Ave., New York, NY 10021 USA
SO Biochemistry, (1997) Vol. 36, No. 31, pp. 9523-9531.
ISSN: 0006-2960.
DT Article
LA English
AB Mechanisms contributing to altered heterotrimeric G-protein expression and subsequent signaling events during cholesterol accretion have been unexplored. The influence of cholesterol enrichment on G-protein expression was examined in cultured smooth muscle cells that resemble human atherosclerotic cells by exposure to cationized LDL (cLDL). cLDL, which increases cellular free and esterified cholesterol 2-fold and 10-fold, respectively, reduced the cell membrane content of G-alpha-i-1, G-alpha-i-2, G-alpha-i-3, Gq/11, and G-alpha-s. The following evidence supports the premise that the mechanism by which this occurs is due to reduced isoprenylation of the G-gamma-subunit. First, the inhibitory effect of cholesterol enrichment on the membrane content of G-alpha-i subunits was found to be post-transcriptional, since the mRNA steady-state levels of G-alpha-i(1-3) were unchanged following cholesterol enrichment. Second, the membrane expression of alpha and beta subunits was mimicked by cholesterol and 17-ketocholesterol, both of which inhibit HMG-CoA reductase. Third, inhibition of G-alpha-i and G-beta expression in cholesterol-enriched cells was overcome by mevalonate, the immediate product of HMG-CoA reductase. Fourth, pulse-chase experiments revealed that cholesterol enrichment did not reduce the degradation rate of membrane-associated G-alpha-i subunits. Fifth, cholesterol enrichment also reduced membrane expression of G-gamma-5, G-gamma-7-upper; these gamma subunits are responsible for trafficking of the heterotrimeric G-protein complex to the cell membrane as a result of HMG-CoA reductase-dependent post-translational lipid modification (geranylgeranylation) and subsequent membrane association. Cholesterol enrichment did not alter expression of G-gamma-5 mRNA, as assessed by reverse transcriptase **polymerase** chain reaction, supporting a post-transcriptional defect in G-gamma subunit expression. Fifth, cholesterol enrichment also reduced the membrane content of p21ras (a low molecular weight G-protein requiring farnesylation for **membrane** targeting) but did not **alter** the **membrane** content of the two proteins that do not require isoprenylation for membrane association-PDGF-receptor or p60-src. Reduced G-protein content in cholesterol-laden cells was reflected by reduced G-protein-mediated signaling events, including ATP-induced GTPase activity, thrombin-induced inhibition of cyclic AMP accumulation, and MAP kinase activity. Collectively, these results demonstrate that cholesterol

enrichment reduces G-protein expression and signaling by inhibiting isoprenylation and subsequent membrane targeting. These results provide a molecular basis for altered G-protein-mediated cell signaling processes in cholesterol-enriched cells.

IT Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular System (**Transport** and Circulation); Cell Biology

IT Chemicals & Biochemicals
CHOLESTEROL; CYCLIC AMP

IT Miscellaneous Descriptors
ARTERIAL SMOOTH MUSCLE CELLS; BIOCHEMISTRY AND BIOPHYSICS; CARDIOVASCULAR SYSTEM; CELL SIGNALING; CHOLESTEROL; CIRCULATORY SYSTEM; CYCLIC AMP; EXPRESSION; G-GAMMA-5 MESSENGER RNA; G-GAMMA-5 MRNA; G-PROTEIN; LDL; LOW DENSITY LIPOPROTEIN; **MEMBRANE** ASSOCIATED; **MEMBRANES**; P21RAS

ORGN Super Taxa
Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rabbit (Leporidae); rat (Muridae)

ORGN Organism Superterms
animals; chordates; lagomorphs; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

RN 57-88-5 (CHOLESTEROL)
60-92-4 (CYCLIC AMP)

L15 ANSWER 22 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:260673 BIOSIS
DN PREV199698816802
TI **Alterations** in adhesion, **transport**, and **membrane polymers** in adhesion-deficient pseudomonads.
AU Oppenheimer, Stephanie R. (1); Condee, Charles C.; Fletcher, Madilyn (1); Deflaun, Mary F.
CS (1) Cent. Marine Biotechnol., Univ. Maryland Biotechnol. Inst., Baltimore, MD 21202 USA
SO Abstracts of the General Meeting of the American Society for Microbiology, (1996) Vol. 96, No. 0, pp. 405.
Meeting Info.: 96th General Meeting of the American Society for Microbiology New Orleans, Louisiana, USA May 19-23, 1996
ISSN: 1060-2011.
DT Conference
LA English

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; **Membranes** (Cell Biology); Methods and Techniques; Physiology

IT Miscellaneous Descriptors
ANALYTICAL METHOD; CELL SURFACE CHARACTERISTICS; ELECTROPHORESIS; LATERAL DISPERSION; MEETING ABSTRACT; OUTER **MEMBRANE** PROTEINS; WILD TYPE

ORGN Super Taxa
Pseudomonadaceae: Eubacteria, Bacteria

ORGN Organism Name
Pseudomonadaceae (Pseudomonadaceae)

ORGN Organism Superterms
bacteria; eubacteria; microorganisms

L15 ANSWER 23 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:123662 BIOSIS
DN PREV199698695797
TI Laboratory markers as an index of aging.

AU Narayanan, Sheshadri N.
CS Dep. Pathol., New York Med. Coll., Metropol. Hosp. Cent., New York, NY 10029 USA
SO Annals of Clinical and Laboratory Science, (1996) Vol. 26, No. 1, pp. 50-59.
ISSN: 0091-7370.
DT Article
LA English
AB At the cellular level, mutations in deoxyribonucleic acid (DNA) can lead to synthesis of altered proteins which are unable to sustain specific cell functions, eventually leading to its death. Veritably apoptosis, or programmed cell death, is a device to eliminate heavily mutated cells. Cell **membranes** with **altered** proteins can be recognized as foreign by the immune system, thus triggering autoimmunity. Molecular biology techniques allow us to examine changes that occur in DNA, reflected by polymorphisms and variable numbers of tandem repeats (VNTR). A general decline in organ function is associated with aging. However, these changes may also be precipitated by disease processes. Homeostatic control by the hypothalamus-pituitary-adrenal axis is also compromised with aging, leading to an increase in plasma adrenocorticotrophic hormone (ACTH) and corticosteroid levels. Derangement of the immune system with aging results in dysregulation of cytokine production. The ability of the cell to survive the onslaught of oxygen-free radicals with enzymatic and nonenzymatic antioxidants, and to repair DNA by activation of nuclear enzymes such as poly (ADP-ribose) **polymerase** (PAD-PRP), are some of determinants of aging.
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (**Transport** and Circulation); Cell Biology; Clinical Chemistry (Allied Medical Sciences); Clinical Immunology (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Geriatrics (Human Medicine, Medical Sciences); **Membranes** (Cell Biology); Metabolism; Pathology; Toxicology
IT Chemicals & Biochemicals
OXYGEN-FREE RADICAL; POLY (ADP-RIBOSE) **POLYMERASE**; ACTH
IT Miscellaneous Descriptors
ANTIOXIDANT; APOPTOSIS; AUTOIMMUNITY; CELL **MEMBRANE**; CYTOKINE PRODUCTION; DNA MUTATION; ENZYMATIC ANTIOXIDANT; NUCLEAR ENZYME ACTIVATION; OXYGEN-FREE RADICAL; PLASMA ACTH LEVEL; POLY (ADP-RIBOSE) **POLYMERASE**; SERUM CORTICOSTEROID LEVEL
ORGN Super Taxa
Hominidae; Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 11062-77-4 (OXYGEN-FREE RADICAL)
9055-67-8 (POLY (ADP-RIBOSE) **POLYMERASE**)
9002-60-2 (ACTH)

L15 ANSWER 24 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:31359 BIOSIS
DN PREV199698603494
TI Deoxygenation-induced **alterations** in sickle cell **membrane** cholesterol exchange.
AU Kavecansky, Juraj; Schroeder, Friedhelm; Joiner, Clinton H. (1)
CS (1) Children's Hosp. Med. Center, Comprehensive Sickle Cell Center, 3333 Burnet Ave., Cincinnati, OH 45229-3039 USA
SO American Journal of Physiology, (1995) Vol. 269, No. 5 PART 1, pp.

C1105-C1111.
ISSN: 0002-9513.
DT Article
LA English
AB Changes in a membrane sterol exchange of sickle red blood cells (SS RBC) induced by deoxygenation were studied using the fluorescent cholesterol analogue dehydroergosterol (DHE). DHE uptake by SS RBC membrane was measured by the incubation of SS RBC with small unilamellar vesicles (SUV) containing DHE. Deoxygenation of SS RBC, but not normal RBC, increased the rate of DHE uptake. DHE membrane content after 5 h of incubation with SUV in the cell-to-SUV ratio of 1:1 (mol lipid) was 16.25 +- 0.94 and 12.22 +- 0.85% of total sterol for deoxygenated and oxygenated cells, respectively. Membrane spicules isolated from these deoxygenated SS RBC had threefold higher DHE content, suggesting that the increased sterol exchange was localized to spicules. When isolated spicules were incubated with DHE-SUV directly, 91 +- 3% of membrane sterol was rapidly exchanged, in contrast to intact RBC, in which a maximum of 33% of sterol could be exchanged. The results suggest that spicule formation in SS RBC **alters membrane** cholesterol structure, such that a domain of cholesterol that is normally nonexchangeable becomes readily exchangeable with exogenous sterol.
IT Major Concepts
Blood and Lymphatics (**Transport** and Circulation); Cell Biology; **Membranes** (Cell Biology); Metabolism; Morphology
IT Chemicals & Biochemicals
CHOLESTEROL
IT Miscellaneous Descriptors
HEMOGLOBIN S **POLYMERIZATION**; UNILAMELLAR VESICLE
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 57-88-5 (CHOLESTEROL)

L15 ANSWER 25 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:402152 BIOSIS
DN PREV199598416452
TI Evaluation by histology, immunohistology and PCR of protocollized renal biopsies 1 week post-transplant in relation to subsequent rejection episodes.
AU Kooijmans-Coutinho, M. F. (1); Bruijn, J. A.; Hermans, J.; Schindler, R.; Frei, U.; Schrama, E.; Van Es, L. A.; Daha, M.r.; Van Der Woude, F. J.
CS (1) Leiden Univ. Hosp., Dep. Nephrol., Build. 1, C3-P, P.O. Box 9600, 2300 RC Leiden Netherlands
SO Nephrology Dialysis Transplantation, (1995) Vol. 10, No. 6, pp. 847-854.
ISSN: 0931-0509.
DT Article
LA English
AB Renal biopsies were performed 1 week following renal transplantation at a time without clinical evidence of rejection in 43 patients (13 females, mean age 48 years range 18-60 and 30 males, mean age 43 years range 17-59 years). Thirty-six biopsies were available for histological or immunohistochemical analysis. Immunohistochemical analyses were performed with monoclonal antibodies against leukocytes (CD45), monocytes (WT14), complement factor 3 (C3), T-cells (Leu4), T-cell receptor alpha-beta and gamma-delta, tumour necrosis factor alpha (TNF-alpha), IL-2 receptor (IL2-R, TAC), intercellular adhesion molecule-1 (ICAM1) and HLA-DR. The slides were scored semiquantitatively with the observers having no

knowledge of clinical or patient data. TNF-alpha and IL-2R were also measured by quantitative PCR. None of the studied parameters correlated to delayed graft function or graft loss. Histological analysis showed that both focal interstitial infiltrate (18/35) and tubular basement **membrane disruption** (11/35) were followed by a higher incidence of subsequent rejection (P = 0.03 and 0.02 respectively). Also positivity for WT14 around tubuli (P=0.02) was associated with subsequent occurrence of rejection. The intensity of staining of ICAM-1 on PTC as well as TAC on proximal tubular cells was associated with the number of subsequent rejection episodes. The association between the IL-2 receptor and subsequent rejection was also found applying PCR to the tissue specimens. We conclude that the presence of focal interstitial infiltrates and tubulitis in 1-week biopsies from well-functioning grafts carries an increased risk of subsequent rejection. The observed infiltrate outside the tubuli may consist of either monocytes or lymphocytes. Further studies, both in vitro and in vivo, applying immunohistochemical and molecular biological techniques will be necessary to further elucidate the role of adhesion molecules and interleukins in early and ongoing rejection.

IT Major Concepts
Blood and Lymphatics (**Transport** and Circulation); Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); **Membranes** (Cell Biology); Methods and Techniques; Physiology; Surgery (Medical Sciences); Urology (Human Medicine, Medical Sciences)

IT Miscellaneous Descriptors
INTERLEUKIN-2 RECEPTOR; INTRACELLULAR ADHESION MOLECULE-I; LYMPHOCYTE; MACROPHAGE; MONOCYTE; **POLYMERASE** CHAIN REACTION; RENAL TRANSPLANTATION

ORGN Super Taxa
Hominidae; Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

L15 ANSWER 26 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:315130 BIOSIS
DN PREV199497328130
TI Twenty seven nucleotide deletion within exon 11 of the erythrocyte band 3 gene in Indonesian ovalocytosis.
AU Takeshima, Yasuhiro (1); Sofro, Abdul Salam; Suryantoro, Purnomo; Narita, Naoko (1); Matsuo, Masafumi (1)
CS (1) Div. Genetics, International Center Med. Res., Kobe University Sch. Med., Kobe Japan
SO Japanese Journal of Human Genetics, (1994) Vol. 39, No. 1, pp. 181-185. ISSN: 0021-5074.
DT Article
LA English
AB We here report the molecular characterization of an Indonesian ovalocytosis. The analysis of genomic gene by **polymerase** chain reaction shows that the individual has two amplified products from a region encompassing exon 11 of the erythrocyte band 3 gene. The sequence of the larger product matched completely with that of normal individuals. In the sequence of the smaller product, 27 nucleotides within exon 11 disappeared. The deletion removes a total of nine amino acids in the boundary of cytoplasmic and membrane domains of band 3 protein, a membrane anion **transporter** protein. This is the first report to confirm

the heterogeneous presence of an **altered membrane** band 3 protein in Indonesian ovalocytosis.

IT Major Concepts
Anthropology; Blood and Lymphatics (**Transport** and Circulation); Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Genetics; **Membranes** (Cell Biology)

IT Miscellaneous Descriptors
MEMBRANE ANION **TRANSPORTER** PROTEIN; MOLECULAR CHARACTERIZATION; **POLYMERASE** CHAIN REACTION

ORGN Super Taxa
Hominidae; Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

L15 ANSWER 27 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1992:231281 BIOSIS
DN BA93:119306
TI DEFECTIVE ANION **TRANSPORT** ACTIVITY OF THE ABNORMAL BAND 3 IN HEREDITARY OVALOCYTIC RED BLOOD CELLS.
AU SCHOFIELD A E; REARDON D M; TANNER M J A
CS DEP. BIOCHEM., SCH. MED. SCI., UNIV. BRISTOL, BRISTOL BS8 1TD, UK.
SO NATURE (LOND), (1992) 355 (6363), 836-838.
CODEN: NATUAS. ISSN: 0028-0836.
FS BA; OLD
LA English
AB Hereditary ovalocytosis is common in some areas of Melanesia and South East Asia where malaria is endemic. These red cells resist invasion by malarial parasites in vitro1,2 and ovalocytic individuals are less parasitized than normal3. This has been attributed to greater rigidity of ovalocytic red cells4,5. It has been suggested that South East Asia ovalocytosis results from the heterozygous presence of an **altered membrane** anion **transporter** (band 3)6,7. We have used the **polymerase** chain reaction to clone the abnormal band 3 complementary DNA from an ovalocytic of Indian origin8 and found two changes from the normal protein: a point mutation (Lys 56 .fwdarw. Glu) and the deletion of the sequence AFSPQVLAA (residues 400-408), but no evidence for an N-terminal extension7. The deletion is also found in the abnormal band 3 of South East Asian ovalocytes9 and seems to be responsible for the unusual properties of the ovalocytic red cell. We show here that the membrane domain of the abnormal ovalocyte band 3 has a substantially altered structure and that the protein is defective in anion **transport** activity. The changed **transport** properties of the red cells may have a role in the reduced parasitaemia of ovalocytic individuals.

IT Miscellaneous Descriptors
HUMAN **ALTERED MEMBRANE** FUNCTION POINT MUTATION SEQUENCE DELETION ENDEMIC MALARIA REGION REDUCED PARASITEMIA **POLYMERASE** CHAIN REACTION MELANESIA SOUTHEAST ASIA

L15 ANSWER 28 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1989:221221 BIOSIS
DN BA87:112838
TI SUPRAMOLECULAR SURFACTANTS AMPHIPHILIC **POLYMERS** DESIGNED TO **DISRUPT** LIPID **MEMBRANES**.
AU REGEN S L; JAYASURIYA N; FABIANOWSKI W
CS DEP. CHEM., LEHIGH UNIV., BETHLEHEM, PA. 18015.
SO BIOCHEM BIOPHYS RES COMMUN, (1989) 159 (2), 566-571.
CODEN: BBRCA9. ISSN: 0006-291X.

FS BA; OLD
LA English
AB Simple polyesters derived from poly(ethylene glycol)s and .alpha., .omega.-dicarboxylic acids exhibit a broad range of activity in **disrupting** phospholipid **membranes**. This activity has been analyzed by measuring the release of liposome-encapsulated 5(6)-carboxy-fluorescein (CF). Comparison with an analogous monomeric surfactant, and with Triton X-100, demonstrate that macromolecular activity is a sensitive function of the size of the **hydrophobic** and **hydrophilic** segments within each repeat unit, and that high disrupting power is possible. In vitro studies with the human immunodeficiency virus type-1 have revealed that those polyesters which exhibit the highest **membrane disrupting** power also provide significant protection for human CD4+ lymphocytes against HIV-1. The potential for adjusting and utilizing these "supramolecular surfactants" in medicine is briefly discussed.
IT Miscellaneous Descriptors
HUMAN IMMUNODEFICIENCY VIRUS LYMPHOCYTE VIRAL DEACTIVATION

L15 ANSWER 29 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1980:165122 BIOSIS
DN BA69:40118
TI PHOTO REGULATION OF THE INCORPORATION OF GUAIACYL UNITS INTO LIGNINS.
AU GRAND C; RANJEVA R; BOUDET A M; ALIBERT G
CS CENT. PHYSIOL. VEG., LAB. ASSOC. FRANCE, CNRS 241, LL8 ROUTE NARBONNE, F-3L077 TOULOUSE CEDEX, FR.
SO PLANTA (BERL), (1979) 146 (3), 281-286.
CODEN: PLANAB. ISSN: 0032-0935.
FS BA; OLD
LA English
AB When fed with [14C] phenylalanine in the light, xylem tissues isolated from poplar (Populus .times. euramericana) stems were able to incorporate part of the radioactivity into both the guaiacyl and the syringyl residues of lignins. In the dark, only syringyl units were integrated into the **polymer** whereas the guaiacyl residues remained unlabeled. When a membrane perturber (isopropanol) was added to the incubation mixture, the label was incorporated into the guaiacyl units either in the light or in the dark. Conversely, a membrane stabilizer (CaCl2) prevented the labeling of the guaiacyl units even when the tissues were illuminated. These results suggest that light acts through the modification of **membrane** permeabilities, **altering** specifically the synthesis and the **transport** or the **polymerization** of guaiacyl-type units during the process of lignification.
IT Miscellaneous Descriptors
POPULUS-EURAMERICANA CARBON-14 PHENYL ALANINE **MEMBRANE** PERMEABILITY SYNTHESIS **TRANSPORT**
RN 9005-53-2D (LIGNINS)
14762-75-5 (CARBON-14)
63-91-2Q, 3617-44-5Q (PHENYL ALANINE)